

Regulation of Novel biomedical Technologies:

- 1. On Presidents, Agencies and the Stem Cells Between Them: A Legal Analysis of President Bush's and the Federal Government's Policy on the Funding of Research Involving Human Embryonic Stem Cells**
- 2. The Regulation of the Genetic Aspects of Donated Reproductive Tissue: The Need for Federal Regulation**
- 3. Patents Versus Statutory Exclusivities in Biological Pharmaceuticals – Do We Really Need Both?**

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ABSTRACT

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This dissertation is the compilation of three separate works of research revolving around the theme of regulation of biomedical technologies that are either emerging or that have undergone significant developments over the past decade or so. Each of these three research works examines a legal response to a technological development in the areas of biotechnology and/or medicine and addresses one or more challenges – ethical, constitutional, legal or one that is related to public policy – created by that response.

The first work of research, which was published in the *Administrative Law Review* in March 2008, examines the legality of the restrictions imposed by the administration of President George W. Bush on the funding of research involving human embryonic stem cells. Reaching the conclusion that the Bush Administration's actions were outright illegal in more than one way, the research highlights existing tensions in the division of decision-making power between the President and executive agencies and between Congress and the President.

The second work of research, which was published in the *Columbia Science and Technology Law Review* in August 2010, reviews the regulation of genetic screening and testing

of donated reproductive tissue in the United States. Analyzing the regulation in the federal, state and industry level, the research highlights significant shortcomings of the regulation of this area and, drawing on the experience of other countries, advocates the regulation of this area by the FDA.

The third and last work of research of which this dissertation consists is dedicated to the examination of the newly created regime of statutory exclusivities afforded to biological pharmaceuticals under the Biologics Price Competition and Innovation Act (BPCIA) as it compares to the protection afforded to such products under patent law. The research concludes that allowing biological pharmaceuticals to benefit from parallel protection under both patent law and the statutory exclusivities regime established under BPCIA does not contribute to incentivizing innovation and might have undesirable ramifications from a public policy perspective. Hence, the research proposes limiting the protection afforded to biological pharmaceutical products, namely to the protection under either patent law or BPCIA, by suspending the ability to enforce patents covering biological pharmaceuticals against generic applicants under BPCIA. In addition, the research examines the proposition that under some circumstances it would be possible to substitute patent protection for statutory exclusivities.

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In loving memory of my grandparents, Chanka (Khanna) Heled of the house of Lewinson and Józef (Yosef) Heled (formerly Chludniewicz), and in memory of all of the members of my family who perished in the Holocaust.

ON PRESIDENTS, AGENCIES, AND THE STEM CELLS BETWEEN THEM: A LEGAL ANALYSIS OF PRESIDENT BUSH'S AND THE FEDERAL GOVERNMENT'S POLICY ON THE FUNDING OF RESEARCH INVOLVING HUMAN EMBRYONIC STEM CELLS

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ABSTRACT

On August 9, 2001, President George W. Bush announced his policy on research involving human embryonic stem cells and proclaimed that federal funding would be allocated only to research involving human embryonic stem cell lines produced prior to his announcement (the Directive). Immediately thereafter, the National Institutes of Health (NIH) announced that it would act in accordance and full compliance with the Directive and took action to implement it. Since then, the Directive has dictated the nature and extent of scientific research involving human embryonic stem cells. Yet, astonishingly, despite being the subject of a boisterous debate, the Directive's legality as well as the legality of the NIH's actions have never been questioned nor ascertained. This Article seeks to fill this gap.

After analyzing the Directive and the NIH's ensuing actions in light of the NIH Revitalization Act of 1993 and the Administrative Procedure Act, this Article argues that the Directive and the NIH's actions taken to

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implement it were illegal. Based on this conclusion, the Article discusses the possible legal challenges that may be raised with respect to the Directive and the NIH's actions.

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INTRODUCTION

On August 9, 2001 at about 8:00 p.m., surrounded by families of children conceived from embryo donations and by members of Congress, President George W. Bush addressed the nation from his ranch in Crawford, Texas and announced his new policy on federal funding for research involving human embryonic stem cells (hESCs).¹ President Bush started by describing the deep religious and ethical sentiments that brought him to make this policy decision² and ultimately proclaimed that federal funding would be allocated only to research involving hESC lines produced prior to his Address.³ Immediately following President Bush's Address, the Acting Director of the National Institutes of Health (NIH), Dr. Ruth Kirschstein, and the Secretary of Health and Human Services (HHS), Tommy G. Thompson, both released statements announcing that they would act in accordance and in full compliance with the Directive.⁴ And so, President Bush's Directive became "the law of the land" and stands unwavering at the crux of the Federal Government's policy regarding the funding for research involving hESCs.

The Directive and subsequent policies adopted by the Bush Administration have been the topic of a multitude of articles dealing with their ramifications. The Directive has inspired an abundance of state legislation either embracing the decision or rejecting and undermining it.⁵ The Bush Administration's policies even became one of the focal points of Senator John Kerry's presidential election campaign in 2004 and of the

1. President George W. Bush, Address to the Nation on Stem Cell Research, 2 PUB. PAPERS 953 (Aug. 9, 2001) [hereinafter President Bush's Address]. I will subsequently refer to this speech as President Bush's Address, President Bush's Stem Cell Decision, or President Bush's Directive.

2. *Id.* at 955 ("My position on these issues is shaped by deeply held beliefs. I'm a strong supporter of science and technology I also believe human life is a sacred gift from our Creator.").

3. *See id.* ("I have concluded that we should allow Federal funds to be used for research on these existing stem cell lines, where the life and death decision has already been made.").

4. *See* Press Release, Ruth Kirschstein, Acting Director of the National Institutes of Health, NIH Statement on the President's Stem Cell Address (Aug. 9, 2001), available at <http://www.nih.gov/news/pr/aug2001/od-09.htm> [hereinafter Kirschstein Statement] (describing President Bush's Decision as "sound" and expressing "understand[ing of] the President's clear desire to move forward with care"); Press Release, Tommy G. Thompson, Secretary, Dep't of Health and Human Servs., Regarding the President's Decision on Human Embryonic Stem Cell Research (Aug. 9, 2001), available at <http://www.hhs.gov/news/press/2001pres/20010809.html> [hereinafter Thompson Statement] (praising the President's decision as a courageous one that shows leadership and stating that he would be proud to carry it out).

5. *See generally* Lauren Thuy Nguyen, *The Fate of Stem Cell Research and a Proposal for Future Legislative Regulation*, 46 SANTA CLARA L. REV. 419, 433-37 (2006) (detailing efforts in some states such as California and New Jersey to protect and endorse stem cell research funding).

Democratic Party's platform in the recent congressional elections.⁶ Yet, with all that has been written and said about President Bush's Directive and the policies implementing it, the focus was always on the economical, ethical, scientific, and social implications and justifications; quite astonishingly, their legality seems to have never been questioned or analyzed.⁷ This Article seeks to fill this void by answering the question whether President Bush's Directive and the Administration's policy on funding for research involving hESCs is legal.

Part I of this Article provides the scientific background necessary for understanding President Bush's Directive and surveys the regulatory history of research involving embryos and hESCs in the United States. Part II then examines and evaluates the validity of President Bush's Directive and of the ensuing actions taken by the NIH, arguing that they were illegal and not legally sustainable. Part III then discusses the possible legal challenges that may be raised with respect to the Directive and the NIH's actions. This Article concludes with predictions about the future of the regulation of research involving hESCs.

I. HUMAN EMBRYONIC STEM CELLS—SCIENTIFIC AND REGULATORY BACKGROUND

A. *Human Embryonic Stem Cells and Their Uses in Medicine and Science*

Prior to delving into the legal discussion, it may be helpful to review what embryonic stem cells are, their scientific purpose and medical potential, and why they incite such a bitter ethical debate.

Stem cells in general (rather than embryonic stem cells) are living cells that are unspecialized; namely, they have not (yet) undergone a process called "differentiation," which turns them into cells that fulfill a specific

6. See, e.g., Charlie Savage, *Stem Cell Issue Opens Campaign Divide*, BOSTON GLOBE, Aug. 8, 2004, at A1; Dan Vergano, *Stem-Cell Debate Another Division Between Bush, Kerry*, USA TODAY, Oct. 26, 2004, available at http://www.usatoday.com/news/politics/nation/issues/2004-10-26-stem-cell-research_x.htm.

7. A number of articles have dealt with the issue of the legality of President Bush's Directive indirectly by analyzing it alongside similar administrative and presidential actions. See, e.g., Tara L. Branum, *President or King? The Use and Abuse of Executive Orders in Modern-Day America*, 28 J. LEGIS. 1, 45-47 (2002) (classifying President Bush's Directive as improper because it did not leave the issue for Congress to decide); Christopher S. Yoo, Steven G. Calabresi & Anthony J. Colangelo, *The Unitary Executive in the Modern Era, 1945-2004*, 90 IOWA L. REV. 601, 725-26 (2005) (praising President Bush's Directive for what the authors view as being exemplary of his leadership and strong principled pro-life stance). However, President Bush's Directive itself was never the focus of an in-depth legal analysis as it is in this Article.

function within the body (e.g., red blood cells, heart-muscle cells).⁸ Under certain conditions, they may undergo differentiation into specialized cell types that are able to fulfill specific bodily functions.⁹ Finally, unlike most of the other cells in our body, stem cells may continue to divide (proliferate) over extended periods of time without “committing” themselves to a certain specialized cell type or function—they may remain in a “stem cell state.”¹⁰

Because of these characteristics, stem cells are a potentially unlimited source of specialized cells for research and for transplantation therapies meant to “replenish” injured tissues that need specific kinds of cells. Some of these therapies, like bone marrow transplantation,¹¹ already exist, while others are currently being researched.¹² Furthermore, because of their special qualities, stem cells may also have other beneficial uses—in research meant to develop methods of prevention and treatment of birth defects; in creation of models, which would make drug development processes faster and cheaper;¹³ and in gene therapy.¹⁴

Stem cells may be subdivided into three classes. The first type of stem cells, with the most differentiation potential, is “totipotent stem cells,” which make up an early embryo, and which are a potential source of any

8. National Institutes of Health (NIH), Stem Cell Basics, I.A., What are stem cells and why are they important?, <http://stemcells.nih.gov/info/basics/basics1.asp> (last visited Oct. 21, 2007) [hereinafter Stem Cell Basics]; NIH, Stem Cell Basics, II., What are the unique properties of all stem cells?, <http://stemcells.nih.gov/info/basics/basics2.asp> (last visited Oct. 21, 2007) [hereinafter Unique Properties of Stem Cells].

9. Stem Cell Basics, *supra* note 8; Unique Properties of Stem Cells, *supra* note 8.

10. Stem Cell Basics, *supra* note 8; Unique Properties of Stem Cells, *supra* note 8.

11. Bone marrow transplantations are essentially stem cell transplantations where patients lacking the capability of replenishing their own blood cells receive hematopoietic stem cells (blood stem cells), which are meant to proliferate and differentiate to replenish the blood cells they need. For further discussion of bone marrow transplantation and other, more modern techniques for acquiring hematopoietic stem cells, see Jos Domen, Amy Wagers & Irving L. Weissman, *Bone Marrow (Hematopoietic) Stem Cells*, in NIH REGENERATIVE MEDICINE REPORT 13, 14, 22 (2006), available at <http://stemcells.nih.gov/info/scireport/2006report.htm> [hereinafter REGENERATIVE MEDICINE].

12. Some of the uses for stem cells, which are currently in the research and development stage, include using stem cells as a source of pancreatic cells for treatment of diabetes, using dopamine-secreting cells for the treatment of Parkinson’s disease, and so forth. See generally *id.* at 13-34; David M. Panchision, *Repairing the Nervous System with Stem Cells*, in REGENERATIVE MEDICINE, *supra* note 11, at 35-44 (discussing how stem cells could be used to treat nervous system disorders); Thomas P. Zwaka, *Use of Genetically Modified Stem Cells in Experimental Gene Therapies*, in REGENERATIVE MEDICINE, *supra* note 11, at 45-52 (illustrating how stem cells can be used in gene therapies for persons with cystic fibrosis and severe combined immunodeficiency).

13. Junying Yu & James A. Thomson, *Embryonic Stem Cells*, in REGENERATIVE MEDICINE, *supra* note 11, at 3 (illustrating how stem cells can help to identify drug targets as well as prevent and treat birth defects). For further information on the uses of human embryonic stem cells (hESCs), see *id.* at 4, 8.

14. See, e.g., NIH, *Use of Genetically Modified Stem Cells in Experimental Gene Therapies*, in STEM CELLS: SCIENTIFIC PROGRESS AND FUTURE RESEARCH DIRECTIONS 99-105 (2001), available at <http://stemcells.nih.gov/staticresources/info/scireport/PDFs/chapter11.pdf> (discussing the benefits of embryonic stem cells in gene therapy).

cell type in an organism's body.¹⁵ The second type of stem cells, with slightly less differentiation potential, is "pluripotent stem cells," also known as embryonic stem cells (ESCs).¹⁶ These cells may be a source of all of the different kinds of cells that make up an organism's body, save early totipotent embryonic cells.¹⁷ Lastly, there are "multipotent stem cells," which have differentiated further than pluripotent stem cells.¹⁸ Within this group of multipotent stem cells are "adult stem cells," which serve as a source of replenishment of cells in the bodies of adult organisms.¹⁹

A general agreement has emerged among leading scientists in the area of stem cell research that research involving pluripotent stem cells holds numerous advantages over research involving adult stem cells.²⁰ Among the reasons for this agreement is the fact that pluripotent stem cells are more readily available²¹ than adult stem cells (which are rare), difficult to extract from the tissues in which they reside, and extremely hard to proliferate while keeping undifferentiated.²² Another reason is that ESCs' low level of commitment makes them potentially more versatile than other, more "committed" stem cells—they may differentiate into more types of specialized cells.²³

15. See NIH, Stem Cell Information, Frequently Asked Questions, <http://stemcells.nih.gov/info/faqs.asp> (last visited Oct. 21, 2007) [hereinafter NIH FAQs] (categorizing stem cells into three classes).

16. *Id.* It is noteworthy that according to recent scientific publications, a group of scientists managed to create hESC lines from totipotent cells rather than from pluripotent cells. See Irina Klimanskaya et al., *Human Embryonic Stem Cell Lines Derived from Single Blastomeres*, NATURE, Nov. 23, 2006, at 481.

17. NIH FAQs, *supra* note 15.

18. *Id.*

19. See NIH, Stem Cell Basics, IV., What are adult stem cells?, <http://stemcells.nih.gov/info/basics/basics4.asp> (last visited Oct. 21, 2007) (describing the differences between adult stem cells and embryonic stem cells).

20. See NIH Statement Before the Senate Appropriations Subcomm. on Labor, Health and Human Services, Education and Related Agencies (Apr. 26, 2000), available at <http://stemcells.nih.gov/policy/statements/state.asp> [hereinafter NIH Statement] (noting that human pluripotent stem cells hold promise for advances in the prevention, treatment, and diagnosis of many diseases).

21. Currently, in the United States there are about 400,000 unused frozen embryos from which embryonic stem cells may be extracted, which, if remain unused for a prolonged period of time, will be disposed of. See Junying Yu & James Thomson, *Embryonic Stem Cells*, in REGENERATIVE MEDICINE, *supra* note 11, at 1, 3.

22. See NIH Statement, *supra* note 20; NIH FAQs, *supra* note 15; NIH, Stem Cell Basics, V., What are the similarities and differences between embryonic and adult stem cells?, <http://stemcells.nih.gov/info/basics/basics5.asp> (last visited Oct. 21, 2007) [hereinafter Embryonic and Adult Stem Cells].

23. NIH Statement, *supra* note 20; NIH FAQs, *supra* note 15; Embryonic and Adult Stem Cells, *supra* note 22.

To be able to utilize ESCs, researchers have to extract these cells from very early embryos and turn them into cell lines²⁴—a process that destroys the embryos.²⁵ This practice, when applied in human embryos, encounters strong opposition on two main grounds. The first is an ethical ground according to which human embryos have a “special moral status” as “early humans,” and thus the practice of destroying such embryos for research purposes constitutes a denial of the respect they are entitled to as an early form of human life. The second ground for opposition is established upon the religious premise that embryos are endowed with God-given life, and that destroying them in the research process constitutes killing. Despite this opposition, since the derivation of the first hESCs in 1998,²⁶ over 120 hESC lines have been created worldwide.²⁷

B. The Regulation of Embryo Research Prior to 1998

Though hESCs were first derived only in 1998, in order to fully understand the regulation of research involving hESCs,²⁸ it is necessary to revisit some constituting events in the regulation of human embryo research, which directly led to and shaped the regulation of research involving hESCs.

24. A cell line is essentially a culture of identical cells that have been transformed in a way that allows them to proliferate in culture indefinitely and that have been kept in that state (of continuous proliferation) for a prolonged period of time. In other words, it is an “immortal” cell culture that will keep on proliferating for as long as it is provided with proper nourishment. This is as opposed to “normal” cells, which proliferate only a limited number of times. For further information on the method of creating ESC lines, see the National Institutes of Health, Stem Cell Basics, III., What are embryonic stem cells?, <http://stemcells.nih.gov/info/basics/basics3.asp> (last visited Oct. 21, 2007). Another method of obtaining pluripotent stem cells is by creating embryos solely for research purposes from egg and sperm donations. *Id.*

25. It is worth noting that some scientists have recently published claims that they have developed methods for creating hESC lines without destroying embryos. See Klimanskaya et al., *supra* note 16, at 481; Xin Zhang et al., *Derivation of Human Embryonic Stem Cells from Developing and Arrested Embryos*, STEM CELLS, Sept. 21, 2006, available at <http://www.StemCells.com/cgi/content/full/24/12/2669>; Constance Holden, *Stem Cells Without the Fuss?*, SCIENCENOW, June 6, 2007; Elizabeth Finkel, *Researchers Derive Stem Cells from Monkeys*, SCIENCENOW, June 19, 2007; Rick Weiss, *Lab Cites Stem Cell Advance: Method of Harvest Could Leave Embryos Undamaged*, WASH. POST, Jan. 11, 2008, at A4. Yet, these publications have encountered skepticism by both proponents and opponents of research involving hESCs. See, e.g., Alison Abbott, *“Ethical” Stem Cell Paper Under Attack*, NATURE, Sept. 7, 2006, at 12; Nicholas Wade, *In New Method for Stem Cells, Viable Embryos*, N.Y. TIMES, Aug. 24, 2006, at A2; Constance Holden, *Life From Arrested Development?*, SCIENCENOW, Sept. 22, 2006; *Scientists Create Stem Cell Line from Already Dead Embryo*, ASSOCIATED PRESS, Sept. 22, 2006.

26. See *infra* note 68.

27. Yu & Thomson, *supra* note 21, at 6.

28. I distinguish between hESC research, which is the research of hESCs, and research involving hESCs, which is any research that makes use of hESCs even for purposes that do not include learning about the hESCs themselves. Since President Bush’s Directive affects both kinds, I will use the latter more inclusive term—research involving hESCs—throughout this Article.

Throughout the 1980s, HHS did not allocate federal funding for research involving human embryos.²⁹ This was because under HHS regulations, funding of such research required the pre-approval of an Ethics Advisory Board (EAB).³⁰ But since the mandate of the last EAB lapsed in 1980³¹ and no new EAB was appointed in its stead, the HHS practically imposed a de facto moratorium on federal embryo research,³² which lasted until Congress passed the NIH Revitalization Act (NIHRA) in 1993.³³

The change in the federal research policy regarding human embryos brought about by the NIHRA can be traced back to a set of events, seemingly unrelated to the aforementioned de facto moratorium, about six years prior to the passing of the NIHRA. In October 1987, the NIH received a request by some of its own investigators to approve a research protocol involving an experimental implantation of human fetal cells taken from aborted human embryos into the brain of a Parkinson's patient.³⁴ Because of the "broad scientific and ethical implications surrounding this area of research,"³⁵ although there was no existing regulatory barrier posed before such research at that time, the Director of the NIH voluntarily decided to request the approval of the Assistant Secretary for Health (ASH) to support this study.³⁶ On March 22, 1988, the Assistant Secretary announced that he was withholding approval of the project and placed a temporary moratorium on the federal support of research involving fetal tissue transplantation pending further consideration "of the relevant ethical, legal, and scientific issues by an outside group of experts"³⁷ that "would

29. See THE PRESIDENT'S COUNCIL ON BIOETHICS, MONITORING STEM CELL RESEARCH 23 (2004), available at http://www.bioethics.gov/reports/stemcell/pcbe_final_version_monitoring_stem_cell_research.pdf [hereinafter PRESIDENT'S COUNCIL REPORT] (explaining that members of Congress became concerned about the potential use of aborted fetuses following *Roe v. Wade*).

30. 40 Fed. Reg. 33,526, 33,529 (Aug. 8, 1975); see also 1 NAT'L BIOETHICS ADVISORY COMM'N, ETHICAL ISSUES IN HUMAN STEM CELL RESEARCH 34 (1999), available at <http://bioethics.georgetown.edu/nbac/stemcell.pdf> [hereinafter NBAC REPORT] (describing the Ethics Advisory Board's recommendations with respect to research involving human embryos).

31. NBAC REPORT, *id.* at 34.

32. *Id.*

33. National Institutes of Health Revitalization Act of 1993, Pub. L. No. 103-43, 107 Stat. 122 (1993).

34. NAT'L INSTS. OF HEALTH, REPORT OF THE ADVISORY COMMITTEE TO THE DIRECTOR: HUMAN FETAL TISSUE TRANSPLANTATION RESEARCH 1 (1988) [hereinafter HUMAN FETAL TISSUE REPORT].

35. *Id.*

36. *Id.*; see also NAT'L INSTS. OF HEALTH, THERAPEUTIC HUMAN FETAL TISSUE TRANSPLANTATION RESEARCH ACTIVITIES FUNDED BY THE NATIONAL INSTITUTES OF HEALTH IN FY 1998: REPORT TO CONGRESS PART III (1999), available at <http://ospp.od.nih.gov/policy/fetal.asp> [hereinafter REPORT TO CONGRESS] (stating that the ASH advised the NIH that it was withholding approval of the project pending consideration of the issues from the Human Fetal Tissue Transplantation Research Panel (HFTTRP)).

37. REPORT TO CONGRESS, *supra* note 36.

examine comprehensively the use of human fetal tissue from induced abortions for transplantation” and advise “whether this kind of research should be performed, and if so, under what circumstances.”³⁸ Pursuant to these instructions, the NIH formed the Human Fetal Tissue Transplantation Research Panel (HFTTRP) to the Advisory Committee to the Director (ACD).³⁹ The HFTTRP held numerous meetings and, in December 1988, submitted its report to the ACD.⁴⁰ The HFTTRP found the use of tissue from induced abortions in therapeutic transplantation research to be “acceptable public policy” and proposed guidelines to assure that such research would be conducted in an ethical manner.⁴¹ The ACD unanimously accepted the recommendations⁴² and passed them on to the Director of the NIH, who also accepted them and recommended to the Secretary to lift the moratorium.⁴³ Interestingly, in November 1989, Secretary Louis Sullivan decided to reject these recommendations and continue the moratorium on federal funding for transplantation research involving human fetal tissue indefinitely.⁴⁴

However, Secretary Sullivan’s moratorium did not go unchecked by Congress. Outraged by the Secretary’s actions,⁴⁵ in a clear and rare expression of discontent with the administrative handling of legislatively delegated powers and of legislative intent to promote human embryo research, Congress passed the NIHRA in 1993.⁴⁶ The NIHRA explicitly abolished Secretary Sullivan’s moratorium,⁴⁷ rescinded the requirement for an EAB’s approval of research applications involving embryo research,⁴⁸

38. Human Fetal Tissue Transplantation Research Panel; Advisory Committee to the Director; Meeting, 53 Fed. Reg. 24,500 (June 29, 1988).

39. *Id.* The Advisory Committee to the Director of the NIH was formed in 1966 to “assist the Office of the Director, NIH, in the making of major plans and policies, especially those related to the allocation of NIH funds and resources.” Advisory Committee to the Director, Charter of the ACD, <http://www.nih.gov/about/director/acd/index.htm> (last visited Dec. 2, 2007).

40. HUMAN FETAL TISSUE REPORT, *supra* note 34, at 2.

41. *Id.* at 4-5; *see also* S. REP. NO. 103-2, at 13 (1993) (describing the HFTTRP and its recommendations).

42. HUMAN FETAL TISSUE REPORT, *supra* note 34, at 4-5.

43. S. REP. NO. 103-2, at 13.

44. *Id.* Congress lifted this moratorium in 1993 in the National Institutes of Health Revitalization Act (NIHRA). *See* Michael Specter, *Fetal-Tissue Research Ban Formally Extended; Moral and Ethical Problems Said To Outweigh Possible Benefits*, WASH. POST, Nov. 3, 1989, at A5.

45. S. REP. NO. 103-2, at 13.

46. National Institutes of Health Revitalization Act of 1993, Pub. L. No. 103-43, 107 Stat. 122 (1993).

47. *Id.* § 113, 107 Stat. at 132.

48. *See* S. REP. NO. 103-2, at 12-15. Congress actually turned the HHS’s de facto moratorium on research involving embryos “upside down” so that the default would no longer be that grant applications for research involving embryos could not be accepted unless ethically approved, but rather that such research proposals were eligible for funding unless an independent Ethics Advisory Board explicitly recommended otherwise. For further discussion, *see infra* Part II.B.1.

and imposed restrictions on the HHS's ability to withhold funds for research on ethical grounds so that such a withholding could not take place without the recommendation of an independent EAB.⁴⁹

Following the enactment of the NIHRA, the NIH began to receive applications for funding of research involving human embryos.⁵⁰ The Secretary of HHS at that time, Donna Shalala, aware of the bioethical issues stemming from such research, decided to establish an EAB in accordance with the NIHRA, and instructed the NIH to proceed accordingly.⁵¹ The NIH, acting under these instructions and in accordance with the requirements of the NIHRA,⁵² formed the Human Embryo Research Panel. The Panel's mandate was to "consider various areas of research involving the ex-utero preimplantation human embryo⁵³ and to provide advice as to those areas that (1) [were] acceptable for Federal funding, (2) warrant additional review, and (3) [were] unacceptable for Federal support."⁵⁴ In September 1994, after seven months of work, the Human Embryo Research Panel published its final report and recommendations regarding research involving human embryos.⁵⁵ First, the Panel concluded that in principle, and pending the fulfillment of some preliminary requirements, there were numerous types of research involving preimplanted human embryos that were ethically permissible.⁵⁶ Most importantly, the Panel determined that creation of human embryos solely for research purposes was permissible if such research could not otherwise be conducted and when "a compelling case can be made that [the research] is necessary for the validity of a study that is potentially of outstanding scientific and therapeutic value."⁵⁷ The report also specifically held that research aimed at the development of human embryonic stem cells should

49. National Institutes of Health Revitalization Act of 1993 § 101, 107 Stat. at 126. For further discussion of the NIHRA and its requirements, see *infra* Part II.B.1.

50. See *Doe v. Shalala*, 862 F. Supp. 1421, 1424-25 (D. Md. 1994) ("With the passage of the Revitalization Act, NIH in fact received a number of applications seeking financial support of research. . . .").

51. *Id.*

52. 42 U.S.C. § 289a-1(b)(5) (2000).

53. The Human Embryo Research Panel used the term "ex-utero preimplanted embryo" to describe human embryos that were the result of IVF treatments, which yielded more embryos than the women treated actually cared to have implanted in them and which were therefore kept frozen. See 1 THE NATIONAL INSTITUTES OF HEALTH, REPORT OF THE HUMAN EMBRYO RESEARCH PANEL, at ix (1994).

54. *Id.*

55. *Id.* at x-xx.

56. *Id.* at x-xi, xvii. These preliminary requirements included conditions such as: that the research on the human embryo could not be otherwise accomplished by using alternative means (e.g., experimentation with animals), that strict informed consent requirements had been met, that only the minimum number of embryos possible for the purposes of the research would be used, that the embryos used would not be older than fourteen days, and so forth.

57. *Id.* at xii.

be permitted, subject to the conditions that the source of the embryos used for the creation of the hESCs would be surplus embryos produced for infertility treatments or clinical research and that the progenitors consented.⁵⁸ On December 1, 1994, the NIH's ACD unanimously accepted the Panel's Report,⁵⁹ but on the very next day, President Clinton released a terse statement (President Clinton's Embryo Decision) instructing the NIH not to allocate funds for supporting the creation of embryos for research purposes.⁶⁰ Thus, President Clinton's Embryo Decision negated one of the Panel's most controversial recommendations, namely the creation of embryos exclusively for research purposes. Nevertheless, his Decision did not prohibit research involving surplus embryos left from in-vitro fertilization (IVF) treatments, and so the NIH proceeded to develop guidelines for funding research using embryos not created solely for research purposes.⁶¹ However, on January 26, 1996, before the NIH was

58. *Id.* at xvii. In addition, the Panel recommended *not* to support numerous kinds of research that were deemed to pose "serious ethical concerns," including research involving human cloning, research of embryos beyond the stage of the closure of the neural tube, pre-implantation diagnosis for the purpose of sex selection, development of human-nonhuman chimeras, cross species fertilization, and more. *See id.* at xix-xx.

59. NBAC REPORT *supra* note 30, at 34.

60. *See* William J. Clinton, Statement on Federal Funding of Research on Human Embryos, 30 WEEKLY COMP. PRES. DOC. 2459, 2459-60 (Dec. 2, 1994) [hereinafter President Clinton's Embryo Decision]. President Clinton's Embryo Decision only noted the following:

The Director of the National Institutes of Health has received a report regarding federal funding of research on human embryos. The subject raises profound ethical and moral questions as well as issues concerning the appropriate allocation of Federal funds. I appreciate the work of the committees that have considered this complex issue, and I understand that advances in vitro fertilization research and other areas could derive from such work. However, I do not believe that Federal funds should be used to support the creation of human embryos for research purposes, and I have directed that NIH not allocate any resources for such research. In order to ensure that advice on complex bioethical issues that affect our society can continue to be developed, we are planning to move forward with the establishment of a National Bioethics Advisory Commission over the next year.

Id. President Clinton's Embryo Decision was not backed or followed by any officiating action such as issuing an executive order and was never published in the Federal Register, but rather only in the Weekly Compilation of Presidential Documents. *See id.* at 2459-60. For further discussion of President Clinton's Embryo Decision and its legal status, see *infra* Part III.A. Interestingly, President Clinton repeated the practice of instructing executive agencies not to fund certain kinds of research that he perceived as bioethically problematic at least once more in a statement released to the media and titled "memorandum," where he explicitly directed "that no Federal funds will be used for human cloning." *See* President William J. Clinton, Memorandum on the Prohibition on Federal Funding for Cloning of Human Beings, 33 WEEKLY COMP. PRES. DOC. 281 (Mar. 4, 1997) [hereinafter President Clinton's Cloning Decision].

Ironically, as I will later show, President Bush's Directive seems to have been the spitting image of President Clinton's Embryo Decision.

61. *See* IRENE STITH-COLEMAN, CRS REPORT FOR CONGRESS: HUMAN EMBRYO RESEARCH 2 (1998), available at http://www.law.umaryland.edu/marshall/crsreports/crsdocuments/95-910_STM.pdf (stating that after the President's December 1994 Order, the agency proceeded with plans to develop guidelines to support research using spare embryos); *see also* NBAC REPORT, *supra* note 30, at 34.

able to approve any application for funding embryo research,⁶² Congress passed the Dickey Amendment, which amended the 1996 Departments of Labor, Health and Human Services, and Education and Related Agencies Appropriations Act,⁶³ cutting the NIH's efforts short.

The Dickey Amendment prohibited federal funding for research involving "the creation of a human embryo or embryos for research purposes"⁶⁴ and any research in which "a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death" greater than a measure allowed by the regulations governing research on fetuses in utero.⁶⁵ Congress has passed similar clauses in the respective appropriations bill every year since,⁶⁶ thus rendering research involving the creation, harming, or destruction of human embryos ineligible for federal funding. And since the creation of hESC lines inevitably involves the

62. See PRESIDENT'S COUNCIL REPORT, *supra* note 29, at 25 (noting mildly that Congress "did not endorse this course of action").

63. The Balanced Budget Downpayment Act, I, Pub. L. No. 104-99, § 128(2), 110 Stat. 26, 34 (1996).

64. *Id.* The Dickey Amendment, which was named after former Representative Jay Dickey who originally sponsored it, reiterated President Clinton's Embryo Decision from 1994 and provided it with legislative backing. For further discussion of this point, see *infra* Part III.A.

65. The Balanced Budget Downpayment Act, I, § 128(2), 110 Stat. at 34. The full language of the Amendment includes:

None of the funds made available [in this Act] may be used for—

(1) the creation of a human embryo or embryos for research purposes; or
(2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR 46.208(a)(2) and 42 U.S.C. 289g(b) [of the Public Health Service Act].

For purposes of this section, the phrase "human embryo or embryos" shall include any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes.

Id.

66. See, e.g., Omnibus Consolidated Appropriations Act, Pub. L. No. 104-208, § 512, 110 Stat. 3009-270 (1996); Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, Pub. L. No. 105-78, § 513, 111 Stat. 1467, 1517 (1997); Omnibus Consolidated and Emergency Supplemental Appropriations Act, Pub. L. No. 105-277, § 511, 112 Stat. 2681-386 (1998); Consolidated Appropriations Act, Pub. L. No. 106-113, § 510, 113 Stat. 1501A-275 (1999); Consolidated Appropriations Act—FY 2001, Pub. L. No. 106-554, § 510, 114 Stat. 2763A-71 (2000); Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, Pub. L. No. 107-116, § 510, 115 Stat. 2177, 2219 (2002); Consolidated Appropriations Resolution, Pub. L. No. 108-7, § 510, 117 Stat. 11 (2003); Consolidated Appropriations Act, 2004, Pub. L. No. 108-199, § 510, 118 Stat. 3277 (2004); Consolidated Appropriations Act, 2005, Pub. L. No. 108-447, § 509, 118 Stat. 2809-3163 (2004); Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, Pub. L. No. 109-149, § 509, 119 Stat. 2833-80 (2005).

destruction of a human blastocyst,⁶⁷ the Dickey Amendment has rendered research involving the creation of such hESC lines similarly ineligible for federal funding.⁶⁸

*C. Federal Regulation of Stem Cell Research Between
Two Presidents—1998 to the Present*

The news about the creation of the first hESC line in late 1998 brought about an abundance of regulatory activity aimed at evaluating the moral and legal status of such cells. In November 1998, President Clinton asked his National Bioethics Advisory Commission (NBAC) to “undertake a thorough review of the issues associated with human stem cell research, balancing all ethical and medical considerations.”⁶⁹ In the meantime, it was unclear whether the Dickey Amendment, which excluded the *creation* of hESC lines with federal funding—because such creation inevitably involves the destruction of embryos—also meant that the federal government could not partake in research involving such hESC lines that already existed, and which were created without federal funding.⁷⁰ To answer this question, the Director of the NIH, Dr. Harold Varmus, approached the General Counsel of HHS, Harriet Rabb, and asked for her opinion regarding the legality of federal funding for research involving hESC lines that were created without federal support.⁷¹ On January 15, 1999, in a legal opinion sent to Dr. Varmus, Harriet Rabb opined that the wording of the Dickey Amendment did not prevent the NIH from funding research involving already-created hESC lines because such hESCs—once extracted from an embryo—did not meet the definition of a human embryo, and hence did not fall under the Amendment’s prohibition on the funding

67. See *infra* Part I.A and text accompanying note 25.

68. Congress, however, did not prohibit such research from taking place altogether; it was (and still is) possible for private entities to conduct such research. Hence, when a group of scientists led by Dr. James Thomson from the University of Wisconsin finally managed to create hESC lines from embryos donated by couples undergoing IVF treatments, they did so without federal funding. See James A. Thomson et al., *Embryonic Stem Cell Lines Derived from Human Blastocysts*, *SCIENCE*, Nov. 6, 1998, at 1145-47; see also Statement of Harold Varmus, M.D., Director, NIH, Department of Health and Human Services, Before the Senate Appropriations Subcomm. on Labor, Health and Human Services, Education and Related Agencies (Dec. 2, 1998), available at <http://stemcells.nih.gov/policy/statements/120298.asp> [hereinafter Statement of Harold Varmus] (“Federal funds were not used in either of the experiments that you will hear about today.”).

69. Letter from President William J. Clinton to Dr. Harold Shapiro, Chair of the National Bioethics Advisory Commission (Nov. 14, 1998), reprinted in NBAC REPORT, *supra* note 30, at 88.

70. See PRESIDENT’S COUNCIL REPORT, *supra* note 29, at 27 (describing this confusion).

71. Statement of Harold Varmus, *supra* note 68.

of the destruction of human embryos.⁷² In other words, the Rabb Opinion held that federal funding could be granted for research involving hESCs, so long as the destruction of the embryos that led to the creation of the hESC lines had not been federally funded.⁷³ Pursuant to the Rabb Opinion, the NIH assigned a Working Group to develop guidelines and oversight mechanisms for research involving human stem cells, and announced a withholding of funds for such research⁷⁴ until the Working Group developed such guidelines.⁷⁵

In September 1999, the NBAC at last published the report requested by President Clinton almost one year earlier.⁷⁶ The underlying premise of the NBAC Report was that “although the human embryo and fetus deserve respect as forms of human life, the scientific and clinical benefits of stem cell research should not be foregone.”⁷⁷ In its report, the NBAC recommended, first and foremost, that federal legislation and regulation be changed so as to allow funding for the use and derivation of hESCs from embryos remaining unused after infertility treatments (namely, not embryos created solely for research purposes).⁷⁸ The NBAC further recommended that any donation of such embryos must fulfill numerous requirements, including obtaining informed consent from the embryos’ donors, approaching potential donors only once they had already decided to discard their excess frozen embryos, informing the donors that their embryos would be destroyed, and regulating the entire area of research through “appropriate regulations that include public oversight and review.”⁷⁹

72. See Memorandum from Harriet S. Rabb, General Counsel of the Department of Health and Human Services, to Harold Varmus, M.D., Director, NIH, on Federal Funding for Research Involving Human Pluripotent Stem Cells (Jan. 15, 1999), <http://www.georgetown.edu/research/nrcbl/documents/rabbmemo.pdf> [hereinafter Rabb Opinion]. According to the Rabb Opinion, hESCs are not subject to the definition of an “embryo” under the Dickey Amendment because an embryo is defined under the Amendment as an “organism” whereas scientific and medically accepted definitions of “organism,” namely an individual constituted to carry out all life functions, do not cover hESCs.

73. *Id.* It is noteworthy that even though the Rabb Opinion was accepted as legally valid and as “stay[ing] within the letter of the law,” it was nonetheless criticized for “contradict[ing] both the spirit of the law and the principle that underlies it.” See PRESIDENT’S COUNCIL REPORT, *supra* note 29, at 27; O. Carter Snead, *The Pedagogical Significance of the Bush Stem Cell Policy: A Window into Bioethical Regulation in the United States*, 5 YALE J. HEALTH POL’Y L. & ETHICS 491, 494 (2005).

74. The source of the NIH Director’s authority to announce this (yet another) moratorium on human embryonic research is not clear, especially in light of the provisions of the NIHRA, which explicitly require a prior EAB recommendation to impose such a moratorium. See 42 U.S.C. §§ 289a-1(b)(1), (3) (2000).

75. Statement of Harold Varmus, *supra* note 68.

76. NBAC REPORT, *supra* note 30.

77. *Id.* at xi.

78. *Id.* at iii-iv.

79. *Id.* at iv-ix.

Pursuant to the publication of the NBAC Report, and having considered its recommendations,⁸⁰ the NIH Working Group that was appointed in early 1999⁸¹ finished developing its guidelines for ensuring that NIH-funded hESC research “is conducted in an ethical and legal manner.”⁸² In December 1999, the NIH published these proposed guidelines, calling for comments from the public (Proposed Guidelines).⁸³ The Proposed Guidelines followed the recommendations of the NBAC Report and allowed federal funding for research utilizing hESCs if: (1) the hESCs were derived from surplus embryos that were originally created for infertility treatments; (2) the decision to donate excess embryos was clearly separate from the decision to create the embryos; and (3) the decision to donate was made at the time the donors decided to dispose of the embryos.⁸⁴ The Proposed Guidelines also outlined areas of research involving hESCs that were ineligible for NIH funding, including the derivation of hESCs from human embryos and research on hESCs that were derived from embryos created for research purposes (thus explicitly applying the Dickey

80. Press Release, National Institutes of Health, NIH Publishes Draft Guidelines for Stem Cell Research (Dec. 1, 1999), <http://www.nih.gov/news/pr/dec99/od-01.htm> (last visited Dec. 2, 2007).

81. See NIH, NIH Fact Sheet on Human Pluripotent Stem Cell Research Guidelines (Jan. 2001), <http://stemcells.nih.gov/news/newsarchives/stemfactsheet.asp> (last visited Dec. 2, 2007) [hereinafter NIH Fact Sheet] (“In April 1999, the NIH convened a working group of the Advisory Committee to the Director.”).

82. National Institutes of Health, Draft National Institutes of Health Guidelines for Research Involving Human Pluripotent Stem Cells (December 1999), 64 Fed. Reg. 67,576, 67,576 (Dec. 2, 1999) [hereinafter Proposed Guidelines].

83. *Id.* It is worth noting that since the Proposed Guidelines involved “a matter relating to . . . public property, loans, grants, benefits, or contracts,” the NIH was presumably exempt from following the notice and comment requirements of the Administrative Procedure Act in promulgating them. See Administrative Procedure Act (APA), 5 U.S.C. § 553(a)(2) (2000). However, the NIH, like all other HHS agencies, has been subject since 1971 to a direction by the Secretary of the Department of Health, Education, and Welfare (HEW) to “utilize the public participation procedures of the APA, 5 U.S.C. § 553” regardless of the exemption. See Statement of Policy: Public Participation in Rule Making, 36 Fed. Reg. 2,532, 2,532 (Feb. 5, 1971). As a result of this voluntary election to abide by the notice and comment requirements of § 553, courts have held the HHS to strict compliance with these requirements. See, e.g., *Mt. Diablo Hosp. Dist. v. Bowen*, 860 F.2d 951, 956-57 n.6 (9th Cir. 1988) (“In 1971 . . . the Secretary waived the public benefits exception Rules promulgated by the Secretary after 1971 are therefore subject to the normal section 553 requirements.”); *Cubanski v. Heckler*, 781 F.2d 1421, 1428 (9th Cir. 1986) (“The Secretary voluntarily waived the APA ‘benefits’ exception in 1971 The [HHS] thereby imposed upon itself procedural requirements ‘not required by law’ The Secretary’s waiver has a binding effect independent of the APA.”); *Buschmann v. Schweiker*, 676 F.2d 352, 356 n.4 (9th Cir. 1982); *Humana of S.C., Inc. v. Califano*, 590 F.2d 1070, 1084 (D.C. Cir. 1978) (“[T]he Secretary in 1971 elected to waive the exemption and to submit to the normal requirements of the [APA], and regulations promulgated since that time are subject to mandatory rulemaking procedures.”) (citation omitted). For discussion of the NIH’s compliance with the APA’s requirements in repealing the Guidelines, see *infra* Part II.C.

84. Proposed Guidelines, 64 Fed. Reg. at 67,577. Other requirements set by the Draft Guidelines include strict and detailed informed consent requirements, privacy requirements and more. *Id.* at 67,577-78.

Amendment to the context of research involving hESCs), human-nonhuman research, and various kinds of cloning research.⁸⁵ In addition, as the NBAC recommended, the Proposed Guidelines suggested the creation of mechanisms to oversee research involving hESCs, including a Human Pluripotent Stem Cell Review Group (HPSCRG), which would review applications for research involving hESCs submitted to the NIH.⁸⁶

On August 25, 2000, almost nine months after the publication of the Proposed Guidelines and extensive review of comments received on them,⁸⁷ the NIH published the Guidelines for Research Using Human Pluripotent Stem Cells (Final Guidelines) in the Federal Register.⁸⁸ The Final Guidelines included all the main components of the Proposed Guidelines as mentioned above (including the areas of research ineligible for funding and the establishment of the HPSCRG)⁸⁹ and lifted the moratorium on research using human pluripotent stem cells derived from human embryos that was announced by the Director of the NIH in January 1999.⁹⁰ Yet, it took the NIH almost another seven months to appoint the HPSCRG and start receiving requests for funding for research in accordance with the Final Guidelines.⁹¹ In fact, the process of the regulation of funding for research involving hESCs was so slow, and lingered for so long, that even after more than two years following the initiation of the process by President Clinton and his Director of NIH, it was still not possible to receive federal funding for such research.

85. *Id.* at 67,579.

86. *Id.*

87. During the comment period, “[t]he NIH received approximately 50,000 comments from members of Congress, patient advocacy groups, scientific societies, religious organizations, and private citizens.” See National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells, 65 Fed. Reg. 51,976, 51,976-79 (Aug. 25, 2000) [hereinafter Final Guidelines].

88. *Id.*; see also Press Release, National Institutes of Health, NIH Publishes Final Guidelines for Stem Cell Research (Aug. 23, 2000), <http://www.nih.gov/news/pr/aug2000/od-23.htm> (last visited Dec. 2, 2007) (announcing the publication of the Final Guidelines).

89. Final Guidelines, 65 Fed. Reg. at 51,976-81.

90. *Id.* at 51,976. See *supra* notes 74-75 and accompanying text.

91. See NIH, Approval Process for the Documentation of Compliance with NIH Guidelines on the Use of Human Pluripotent Stem Cells in NIH Research Proposed for Support Under Grants and Cooperative Agreements, Notice OD-02-007 (Nov. 7, 2001), available at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-003.html> [hereinafter Notice OD-02-007] (stating that the first meeting of the Human Pluripotent Stem Cell Review Group (HPSCRG) would take place on March 15, 2001); NIH, Approval Process for the Documentation of Compliance with NIH Guidelines on the Use of Human Pluripotent Stem Cells in NIH Intramural Research (Jan. 16, 2001), available at http://stemcells.nih.gov/news/newsarchives/irpnotice_011601.asp; NIH Fact Sheet, *supra* note 81 (“The NIH is in the process of finalizing the members of the HPSCRG in preparation for a March deadline for the receipt of requests for NIH funding for human pluripotent stem cell research.”).

In January 2001, close to the beginning of President Bush's presidency, the NIH was still dragging its feet regarding the appointment of the HPSCRG in preparation for the submission of research applications involving hESCs, which were due by March 15, 2001.⁹² It soon became clear that the change in office was going to have a radical influence on the administration's policy regarding stem cell research. Almost as soon as President Bush took office, he charged his Secretary of HHS, Tommy Thompson, with conducting a review of the Final Guidelines and with putting the Guidelines "on hold" pending the results of that review.⁹³ In addition, in April 2001, HHS officials ordered the Acting Director of the NIH, Ruth Kirschstein, to indefinitely postpone a scheduled meeting of the newly appointed HPSCRG, which was supposed to review the first applications for research grants under the Final Guidelines,⁹⁴ thus de facto revoking the Final Guidelines.

Although the legality of this de facto revocation was highly questionable,⁹⁵ a district court order upheld and even bolstered the Bush Administration's actions.⁹⁶ On March 8, 2001, a group of plaintiffs consisting of religious groups and pro-life activists filed an action against the Government seeking an order and declaratory relief, which would determine that the Final Guidelines were unlawful and would enjoin the Government from applying them and from funding research involving

92. See Notice OD-02-007, *supra* note 91 (illustrating the schedule for receipt and review by the HPSCRG).

93. PRESIDENT'S COUNCIL REPORT, *supra* note 29, at 28; Gretchen Vogel, *Stem Cell Review Setback*, SCIENCENOW, Apr. 16, 2001.

94. Though such an order or instruction was never officially published, and though it was not known whether Secretary Thompson or President Bush gave this order, the HHS Spokesman, Bill Hall, admitted that such instruction was in fact given and explained that "the department felt that it makes the most sense to hold off until the guideline review that the department is doing is complete." See Rick Weiss, *Bush Administration Order Halts Stem Cell Meeting; NIH Planned Session to Review Fund Requests*, WASH. POST, Apr. 21, 2001, at A2; Nicholas Wade, *Grants for Stem Cell Work Are Delayed*, N.Y. TIMES, Apr. 24, 2001, at F6.

95. According to federal case law "an agency decision which effectively suspends the implementation of important and duly promulgated standards . . . constitutes rulemaking subject to notice and comment requirements of 5 U.S.C. § 553." See *Env'tl. Def. Fund, Inc. v. Gorsuch*, 713 F.2d 802, 816-17 (D.C. Cir. 1983); *Env'tl. Def. Fund, Inc. v. EPA*, 716 F.2d 915, 920 (D.C. Cir. 1983) ("The suspension or delayed implementation of a final regulation normally constitutes substantive rulemaking under APA § 553. Thus . . . [it is] subject to APA notice and comment provisions.") (citations omitted); *Natural Res. Def. Council, Inc. v. EPA*, 683 F.2d 752, 761-63 (3d Cir. 1982) ("[The] EPA's action in indefinitely postponing the effective date of the amendments . . . was subject to the APA's rulemaking requirements."). The Bush Administration's suspension of the Final Guidelines did not meet the notice and comment requirements of the APA. Thus, the suspension of the Final Guidelines was illegal. For further discussion of why the APA's notice and comment requirements apply to the Final Guidelines despite the exemption of matters involving grants or benefits from these requirements, see *supra* note 83.

96. *Nightlight Christian Adoptions v. Thompson*, No. 1:01 CV 00502-RCL (D.D.C. May 4, 2001) (order staying lawsuit).

hESCs.⁹⁷ Ironically, the Bush Administration was apparently only too happy to comply with the Plaintiffs' demands. The Administration quickly yielded to them and entered into a stipulation in which the Administration took it upon itself to avoid: (1) any funding of hESC research; (2) the approval of any application thereof; and (3) the convening of the HPSCRG, at least until the completion of its own review of the Final Guidelines, which was not subject to any timetable.⁹⁸ On May 4, 2001, Judge Lamberth of the District Court cemented the agreement between the parties by entering an order to stay the proceedings subject to the terms of the parties' stipulation.⁹⁹ Thus, the Judge gave his stamp of approval to the Bush Administration's illegal suspension of the Final Guidelines¹⁰⁰ and effectively sealed their indefinite suspension,¹⁰¹ which continues until today.

During the following months, President Bush was engaged in the reexamination of the issue of research involving hESCs. He consulted with clergymen (including the late Pope John Paul II), religious groups, ethicists (including the bioethicists Daniel Callahan and Leon Kass, whom President Bush would later appoint to be the head of his Council on Bioethics), members of Congress, patient groups, and scientists (including a group of NIH scientists who told President Bush that more than sixty-five hESC lines existed at that time).¹⁰²

97. Complaint for Declaratory and Injunctive Relief at 2, *Nightlight Christian Adoptions v. Thompson*, No. 1:01 CV 00502-RCL (D.D.C. Mar. 8, 2001).

98. *Nightlight Christian Adoptions v. Thompson*, No. 1:01 CV 00502-RCL (D.D.C. May 4, 2001) (order staying lawsuit).

99. *Id.*

100. *See supra* note 95.

101. *Id.*; *see also* Joseph Curl, *Judge Halts Stem Cell Research Pending HHS Review*, WASH. TIMES, May 11, 2001, at A3 (summarizing recent political and judicial efforts to curtail stem cell research). It is worth noting that shortly after the *Nightlight* decision, a group of scientists led by the creator of the first hESC lines, Dr. James Thomson, and three patients, including the late actor Christopher Reeve, filed another lawsuit in the same court asking the court to declare the Final Guidelines legal and instruct the government to apply them. *See* Complaint for Declaratory and Injunctive Relief, *Thomson v. Thompson*, No. 1:01-CV-00973-RCL (D.D.C. May 8, 2001); *see also* Gretchen Vogel, *Researchers Sue to Study Stem Cells*, SCIENCE NOW, May 22, 2001. On August 8, 2001, a day before President Bush's Statement, Judge Lamberth landed a final blow to the application of the Final Guidelines by staying this lawsuit "pending the decision by [the Government] whether to provide federal funding for human embryonic stem cell research." *Thomson v. Thompson*, No. 1:01-CV-00973-RCL (D.D.C. Aug. 8, 2001) (order staying lawsuit). Thus, Judge Lamberth's decision practically afforded the government unlimited time to review the Final Guidelines.

102. Richard Lacayo, *How Bush Got There*, TIME, Aug. 12, 2001, at 17; Alessandra Stanley, *Bush Hears Pope Condemn Research in Human Embryos*, N.Y. TIMES, July 24, 2001, at A1. Apparently, the number of hESC lines, which scientists claimed already existed at that time made a crucial impact on the formulation of President Bush's Directive. *See* Lacayo, *supra*.

At this point, with respect to the issue of federal funding for research involving hESCs, President Bush no longer made a distinction between his opinions and those of his Administration. Rather, he viewed the issue as *his own personal matter*, which was to be decided *solely and exclusively by him*. This position was well-reflected in some of President Bush's descriptions of the way he approached the issue of research involving hESCs and in the way he addressed it.¹⁰³ For example, President Bush repeatedly stressed that *he* personally, was the one considering the issue of research involving hESCs, that *he* was the one who encountered the dilemmas involved in this issue, and that *he* was taking *his* time making *his* decision.¹⁰⁴ President Bush's posture in this respect was well-reflected in the language he used in his Address:

I've asked those questions and others of scientists, scholars, bioethicists, religious leaders, doctors, researchers, Members of Congress, my Cabinet, and my friends. I have read heartfelt letters from many Americans. I have given this issue a great deal of thought, prayer, and considerable reflection. And I have found widespread disagreement.

. . . .

My position on these issues is shaped by deeply held beliefs. I'm a strong supporter of science and technology

I also believe human life is a sacred gift from our Creator.

. . . .

I have concluded that we should allow Federal funds to be used for research on these existing stem cell lines

*. . . I have made this decision with great care, and I pray it is the right one.*¹⁰⁵

And so, when President Bush finally made *his* decision with respect to the funding of research involving hESCs, he chose to deliver it directly to *his* constituents in the first televised address he made since taking office.¹⁰⁶

103. See Lacayo, *supra* note 102 ("For a while this year it seemed that George W. Bush buttonholed everybody he met to get his or her view on stem-cell research.").

104. President Bush said: "I take this issue very seriously It's also an issue that has got serious moral implications, and our nation must think carefully before we proceed And, therefore, my process has been, frankly, unusually deliberative for my administration. I'm taking my time." Stanley, *supra* note 102. In another place, President Bush explained his Decision by saying that "[u]nder *my* policy, existing stem cell lines, to be used in publicly supported research, must be derived (1) with the informed consent of donors, (2) from excess embryos created solely for reproductive purposes and (3) without any financial inducements to the donors." See George W. Bush, *Stem Cell Science and the Preservation of Life*, N.Y. TIMES, Aug. 12, 2001, at WK13 [hereinafter *President Bush's Op-Ed Piece*] (emphasis added).

105. President Bush's Address, *supra* note 1, at 954-56 (emphasis added).

106. *Id.*

On August 9, 2001, President Bush delivered his Stem Cell Decision, which allowed only for funding of research involving hESC lines that were: (1) created prior to his Address;¹⁰⁷ (2) made of excess embryos created strictly for reproductive purposes; (3) where the embryos were obtained with the informed consent of the donors; and (4) without any financial inducement to the donors.¹⁰⁸ In addition, President Bush's Directive forbade any funding of research involving the creation of human embryos solely for research purposes and the cloning of human embryos for any purpose.¹⁰⁹

A curious fact about President Bush's Directive is that, unlike most presidential executive orders and directives, it was never published in the Federal Register and was only delivered as a televised Address (along with a Fact Sheet). Failing to publish the Directive seems even stranger in light of the fact that President Bush *did* sign an executive order establishing his new Council on Bioethics, which he also announced in his Address,¹¹⁰ but refrained from doing the same with respect to the crux of his Address, namely the prohibition on funding for research involving hESCs created thereafter.¹¹¹

107. According to the NIH, "prior to his Address" means that the hESC derivation process should have been initiated prior to 9:00 p.m. EDT on August 9, 2001. See NIH Update on Existing Human Embryonic Stem Cells (Aug. 27, 2001), <http://stemcells.nih.gov/policy/statements/082701list.asp> (last visited Dec. 2, 2007) [hereinafter NIH Update].

108. President Bush's Address, *supra* note 1.

109. The White House Fact Sheet: Embryonic Stem Cell Research (Aug. 9, 2001), <http://whitehouse.gov/news/releases/2001/08/20010809-1.html> (last visited Dec. 2, 2007) [hereinafter Fact Sheet]. It is interesting to note that in delivering his decision, President Bush refrained from directly referring to the kinds of research that may not receive federal funding, and used a rhetoric which only addressed the types of research he *would* allow his Administration to fund. The "forbidden" types of research were thus enumerated only in a "fact sheet," which was released concurrent with the Address and which strictly held that "[f]ederal funds will *only* be used for research on existing stem cell lines" and that "[n]o federal funds will be used for . . . the derivation or use of stem cell lines derived from newly destroyed embryos." *Id.* (emphasis added). The use of this language allowed President Bush's Administration and supporters to portray his Decision as actually *allowing funding* for stem cell research rather than withholding such funding. See, e.g., Rick Weiss, *Promising More—and Less; Scientists See Growth in Field, Lament Limits*, WASH. POST, Aug. 10, 2001, at A1; President Council's Report, *supra* note 29, at 28; Testimony of Tommy G. Thompson, Secretary of Health and Human Services Before the Senate Health, Education, Labor and Pensions Comm. (Sept. 5, 2001), *available at* <http://www.hhs.gov/news/speech/2001/010905.html> ("President Bush has opened the laboratory door. Now, let's get our best and brightest scientists into the lab so they can go to work."). However, it is important to note that it was in fact the Administration's actions prior to President Bush's Address that hindered the implementation of the Final Guidelines, which would have probably allowed for such funding much sooner.

110. Exec. Order No. 13,237, 66 Fed. Reg. 59,851 (Nov. 28, 2001). The established Council, which was headed by Dr. Leon Kass and which was mostly manned by members holding a conservative viewpoint, later published its report on stem cell research, which retroactively, ethically endorsed President Bush's Directive. See *generally* PRESIDENT'S COUNCIL REPORT, *supra* note 29.

111. For further discussion of this omission and its possible reasons, see *infra* Part II.A and note 283.

Despite the fact that President Bush did not “formalize” his Directive and did not specifically instruct HHS and the NIH to follow his Stem Cell Decision, within hours of his Address, both Secretary Thompson and the Acting Director of the NIH, Ruth Kirschstein published their endorsement of President Bush’s Directive,¹¹² and thus sealed the fate of the portion of the Final Guidelines that dealt with hESCs.¹¹³ Two weeks after President Bush’s Address, the NIH announced that it was initializing a new process to enable funding of research involving hESCs in accordance with President Bush’s Directive and a prohibition on its intramural investigators (in what was apparently yet another moratorium) to conduct research on any hESCs until the new procedures were in place.¹¹⁴

On November 7, 2001, the NIH officially announced that it was accepting grant applications for research involving hESC lines that complied with President Bush’s Directive¹¹⁵ and the creation of hESC registry, which included all of the hESC lines that met those requirements.¹¹⁶ Notably, around the time of President Bush’s Address, there was some confusion and disagreement regarding the actual number of viable and available hESC lines that complied with President Bush’s Directive.¹¹⁷ To date, the NIH hESC registry includes sixty-seven lines, and only twenty-one are actually available for researchers who wish to apply for federal funding.¹¹⁸

112. Kirschstein Statement, *supra* note 4; Thompson Statement, *supra* note 4.

113. Ironically, it was Ruth Kirschstein who only a year earlier, signed the publication of the Final Guidelines. For further discussion of Ruth Kirschstein’s actions, see *infra* Part II.C.

114. NIH Funding of Research Using Specified Existing Human Embryonic Stem Cells, NOT-OD-01-058 (Aug. 23, 2001), available at <http://grants.nih.gov/grants/guide/notice-files/not-od-01-058.html>, superseded by NOT-OD-01-059 (Aug. 27, 2001).

115. Notice of Extended Receipt Date and Supplemental Information Guidance for Applications Requesting Funding that Proposes Research with Human Embryonic Stem Cells, NOT-OD-02-006 (Nov. 7, 2001), available at <http://grants.nih.gov/grants/guide/notice-files/not-od-02-006.html>; Notice of Criteria for Federal Funding of Research on Existing Human Embryonic Stem Cells and Establishment of NIH Human Embryonic Stem Cell Registry, available at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html>.

116. See NIH, NIH Human Embryonic Stem Cell Registry, <http://stemcells.nih.gov/research/registry> (last visited Dec. 2, 2007) (listing the derivations of stem cells that are eligible for federal funding).

117. While one NIH publication stated that there were sixty-four hESC lines, another mentioned seventy-eight, a third mentioned seventy-one, and so forth. See NIH Update, *supra* note 107 (sixty-four); Department of Health and Human Services, Fact Sheet—Embryonic Stem Cell Research (July 14, 2004), <http://www.hhs.gov/news/press/2004pres/20040714b.html> (seventy-eight); NIH, NIH’s Role in Federal Policy—Stem Cell Research (Aug. 12, 2005), <http://stemcells.nih.gov/policy/NIHFedPolicy.asp> (seventy-one).

118. Yu & Thomson, *supra* note 21, at 6. The discrepancy between the number of hESC lines in the registry and the number of such lines actually available results from various reasons. According to the NIH hESC registry, some of the hESCs never became cell lines due to halted growth or failure to remain undifferentiated. One line was withdrawn by its donor, others are “unavailable for shipping,” and so forth. The number of hESC lines available for research is significantly smaller than the number of such lines President Bush was led to believe were available prior to reaching his Stem Cell Decision, which was

On November 14, 2001, the NIH announced the demise of the parts of the Final Guidelines dealing with funding for research involving hESCs.¹¹⁹ The only reason mentioned by the NIH for the withdrawal of the Final Guidelines was that “[t]he President has determined the criteria that allow Federal funding for research using existing embryonic stem cell lines Thus, the NIH Guidelines as they relate to human pluripotent stem cells . . . are no longer needed.”¹²⁰ This last notice essentially gave the regulatory framework for research involving hESCs its final form as it exists today.

Since August 2001, Congress has tried to change the regulatory scheme of funding for research involving hESCs numerous times¹²¹ without much success.¹²² Most notably, on July 18, 2006, the Senate passed the Stem Cell Research Enhancement Act of 2005.¹²³ This Act was supposed to add § 498D to the Public Health Service Act (PHSA),¹²⁴ which would have instructed the Secretary of HHS to start conducting and supporting research involving hESCs so long as the hESC lines involved in the research complied with the following “ethical requirements”:

- (1) The stem cells were derived from human embryos that have been donated from in vitro fertilization clinics, were created for the purposes of fertility treatment, and were in excess of the clinical need of the individuals seeking such treatment.
- (2) Prior to the consideration of embryo donation and through consultation with the individuals seeking fertility treatment, it was determined that the embryos would never be implanted in a woman and would otherwise be discarded.

actually even smaller at the time he gave his Address—only one or two in the spring of 2002! See *President Bush’s Op-Ed Piece*, *supra* note 104; NIH FAQs, *supra* note 15.

119. National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells, 66 Fed. Reg. 57,107 (Nov. 14, 2001).

120. Notice of Withdrawal of NIH Guidelines for Research Using Pluripotent Stem Cells, NOT-OD-02-007 (Nov. 7, 2001), available at <http://grants.nih.gov/grants/guide/notice-files/not-od-02-007.html>.

121. *E.g.*, Stem Cell Replenishment Act of 2005, H.R. 162, 109th Cong. (2005); Human Cloning Ban and Stem Cell Research Protection Act of 2003, S. 303, 108th Cong. (2003); Science of Stem Cell Research Act, H.R. 4011, 107th Cong. (2002); Stem Cell Research Act of 2001, H.R. 2059, 107th Cong. (2001); Stem Cell Research for Patient Benefit Act of 2001, H.R. 2747, 107th Cong. (2001) (sought to codify the Final Guidelines); New Century Health Advantage Act, H.R. 2838, 107th Cong. (2001) (sought to require the NIH to conduct human embryonic stem cell research and repeal the Dickey Amendment).

122. None of Congress’s bills or acts, save two, were ever voted into law, and the only bills that were actually voted for by both Houses were vetoed by President Bush. See *infra* notes 126-31.

123. Stem Cell Research Enhancement Act of 2005, H.R. 810, 109th Cong (2006).

124. Public Health Service Act, ch. 373, 58 Stat. 682 (1944) (codified as amended at 42 U.S.C. §§ 201-300ii-4 (2000)).

- (3) The individuals seeking fertility treatment donated the embryos with written informed consent and without receiving any financial or other inducements to make the donation.¹²⁵

The passing of the Stem Cell Research Enhancement Act by a Republican Congress¹²⁶ expressed an unequivocal congressional discontent with the current regulatory scheme for funding research involving hESCs, which is based on the policy set by President Bush's Directive. Yet eventually, on July 19, 2006, President Bush vetoed the Stem Cell Research Enhancement Act.¹²⁷ Attempts to raise the two-thirds majority in the House failed and the Act was abandoned.¹²⁸ In 2007, the newly formed Democratic majority in Congress again passed the Stem Cell Research Enhancement Act.¹²⁹ Once more, President Bush vetoed the Act¹³⁰ and there was no two-thirds majority in Congress to override the veto.¹³¹ And so, since President Bush's Address in August 2001, and until today, the only federal funding available for research involving hESCs is for research that uses the twenty-one hESC lines that meet President Bush's Directive's criteria.

II. LEGAL ANALYSIS OF PRESIDENT BUSH'S DIRECTIVE AND HIS ADMINISTRATION'S ENSUING POLICY

Having described the regulatory framework of research involving hESCs, it is now possible to begin its legal examination. The first step in analyzing President Bush's Directive and the NIH's ensuing actions is to identify the type of presidential directive it is and the ramifications of the Directive's form, if any, on its enforceability. Once the question of form is addressed, this Article will discuss the main substantive question of whether President Bush had the legal authority to give his Directive and

125. These requirements are almost identical to those set in President Bush's Directive except for the fact that they do not restrict federal funding to hESC lines created prior to August 9, 2001, at 9:00 p.m. In this respect, the Human Stem Cell Research Enhancement Act of 2005 would have essentially enacted the Final Guidelines into law.

126. Despite the fact that the first session of the 109th Congress was clearly Republican, the Stem Cell Research Enhancement Act of 2005 passed by a majority of 238-194 in the House of Representatives, and 63-37 in the Senate.

127. Press Release, White House, Message to the House of Representatives, 2006 WL 2007324 (July 19, 2006).

128. In a vote in the House of Representatives that same day, the supporters of the Act managed to raise a majority of 235 yeas against 193 nays.

129. On January 11, 2007, the House of Representatives passed a bill identical to the Stem Cell Research Enhancement Act of 2005. *See* Stem Cell Research Enhancement Act of 2007, H.R. 3, 110th Cong. (2007). Three months later, on April 11, 2007, the bill passed in the Senate. *See* S. 5, 110th Cong. (2007).

130. Press Release, White House, President Bush Discusses Stem Cell Veto and Executive Order, 2007 WLNR 11640195 (June 20, 2007).

131. *See* Sheryl Gay Stolberg, *Bush Vetoes Bill Removing Stem Cell Limits, Saying 'All Human Life is Sacred'*, N.Y. TIMES, June 21, 2007, at A21 ("Democrats concede they do not have enough votes for a veto override.").

require the NIH to comply, and—assuming he had such authority—whether he used it appropriately. Finally, if the answer to the previous question is in the affirmative, in order to evaluate the legality of the current regulatory scheme of funding for research involving hESCs, it is necessary to determine whether the NIH’s actions implementing President Bush’s Directive were in accord with the NIH’s own authorities, duties, and responsibilities under the law.

*A. Classification of President Bush’s Directive’s Form and
Evaluation of Its Validity from a Procedural Standpoint*

It is said that presidential directives are the “most elusive in [their] capacity to be legally analyzed and constrained.”¹³² There are over twenty types of such ill-defined presidential directive instruments including, but not limited to: executive orders, proclamations, presidential memoranda, and signing statements.¹³³ In addition, neither the Constitution nor any statute or case law defines exactly what presidential directives are, how to distinguish among their different kinds,¹³⁴ how the President may use them and to what end, what procedural requirements must be fulfilled in using them in general and each of them in particular, and what is the permissible scope of their substance.¹³⁵ The only exceptions are those presidential directives categorized as executive orders and proclamations, which are subject to the Federal Register Act¹³⁶ and to Executive Order No. 11,030.¹³⁷ Therefore, so long as their directives bear forms other than “executive

132. PETER L. STRAUSS, TODD D. RAKOFF & CYNTHIA R. FARINA, *ADMINISTRATIVE LAW: CASES AND COMMENTS* 193 (10th ed. 2003).

133. See Harold C. Relyea, *Congressional Research Service Report for Congress: Presidential Directives: Background and Overview* (2005), available at <http://www.fas.org/irp/crs/98-611.pdf> (providing an overview of the different kinds of directives used by presidents in the twentieth century).

134. See Todd F. Gaziano, *The Use and Abuse of Executive Orders and Other Presidential Directives*, 5 TEX. REV. L. & POL. 267, 282, 290-91 (2001) (discussing the difficulties in discerning between different presidential directives); see also COMMITTEE ON GOVERNMENT OPERATIONS, 85TH CONG., EXECUTIVE ORDERS AND PROCLAMATIONS: A STUDY OF A USE OF PRESIDENTIAL POWERS 1 (1957) [hereinafter CONGRESSIONAL STUDY OF EXECUTIVE POWER] (“There is no law or even Executive order which attempts to define the terms ‘Executive order’ or ‘proclamation.’”).

135. See Gaziano, *supra* note 134, at 282 (emphasizing the broad discretion presidents have in using directives).

136. The Federal Register Act, ch. 417, 49 Stat. 500 (1935) (codified as amended at 44 U.S.C. §§ 1501-1511) (1964), requires that executive orders and proclamations generally be published in the Federal Register. See 44 U.S.C. § 1505(a).

137. Exec. Order. No. 11,030, 27 Fed. Reg. 5847 (June 21, 1962). The Order requires, among other things, that executive orders and proclamations “contain a citation of the authority under which [they are] issued” and that they be submitted to the Attorney General who must approve their substance, form, and legality. *Id.*; see also Gaziano, *supra* note 134, at 292-93 (discussing procedures for issuing proclamations and executive orders).

orders” or “proclamations,” presidents may tailor their directives in any way they want, giving them any title they want, and using them for any means they see fit, without having consequences on the enforceability of the directives from a formal standpoint.¹³⁸

President Bush and his Administration, probably well aware of this situation, seem to have taken advantage of it in designing President Bush’s Directive so as to ensure that its form would be impervious to judicial review.¹³⁹ First, the President delivered his Address orally, on television, and it was never published in the Federal Register.¹⁴⁰ The accompanying Fact Sheet was never published in any formal government publication.¹⁴¹ Second, neither the Address nor the Fact Sheet bears the signature of the President, and the Address does not include any specific operational instructions directed at executive officers, but is merely a vague pronouncement of moral preferences.¹⁴² Finally, the Address and Fact Sheet carry none of the conventional titles, which could have helped to classify them under one of the known forms of presidential directives (e.g., “executive order” or “memorandum”).¹⁴³ Thus, President Bush’s Directive does not seem to fall squarely under any of the known types of

138. According to Gaziano, “a new President and a creative bureaucracy could come up with twenty-four new ‘types’ [of presidential directives] if they wished to do so.” See Gaziano, *supra* note 134, at 291.

139. Had the Administration chosen to issue the Directive in the more conventional form of an executive order, it would have been obliged to state its source of authority as well as to have its content approved by the Attorney General. See *supra* notes 136-37. As I will later show, the Bush Administration would have been hard pressed to do either of these things. See *infra* Part II.B. And so, it is prudent to assume that the Administration’s omission to cement the Stem Cell Decision—which is one of President Bush’s Administration’s landmark policies—in such a duly issued executive order since August 2001 has not been the result of neglect, but rather of a deliberate effort by the Administration to avoid having to state the Directive’s source of authority, which might cast its legal legitimacy in a questionable light.

140. President Bush’s Address was only published in the Weekly Compilation of Presidential Documents, and in the Public Papers of the Presidents of the United States. See President Bush’s Address, *supra* note 1; President George W. Bush, Address to the Nation on Stem Cell Research, 37 WEEKLY COMP. PRES. DOC. 1151 (Aug. 9, 2001).

141. The Fact Sheet seems to be available only through the White House Office of the Press Secretary. See Fact Sheet, *supra* note 109.

142. *Id.* The “operative” part of President Bush’s Directive only surfaces in the accompanying Fact Sheet.

143. The title of the written version of the Address is “President Discusses Stem Cell Research,” and the title of the Fact Sheet is “Fact Sheet: Embryonic Stem Cell Research.” According to Gaziano, the primary method of classification of presidential directives relies almost exclusively on the title they are given. See Gaziano, *supra* note 134, at 288-89; see also CONGRESSIONAL STUDY OF EXECUTIVE POWER, *supra* note 134, at 1; Branum, *supra* note 7, at 7.

presidential directives.¹⁴⁴ As a result, there are no formal or procedural requirements applicable to it, so it cannot suffer from any formal or procedural flaw, which might have affected its validity or enforceability.

*B. Analysis and Evaluation of President Bush's Authority
to Issue His Directive and Enforce It on the NIH*

Similar to the lack of regulation characterizing the formal and procedural aspects of presidential directives, there is very little law regulating the President's authority to issue such directives¹⁴⁵ and how one can evaluate the legality of such directives. Except for the axiomatic premise that presidential acts must be based on a legal source of authority (or else the President would actually be acting as an autocrat),¹⁴⁶ the most important source of guidance on these issues is found in Justice Jackson's famous and highly influential opinion in the matter of *Youngstown Sheet & Tube Co. v. Sawyer*.¹⁴⁷ According to Justice Jackson, when evaluating the legitimacy of presidential actions, a court should weigh the actions' sources of statutory and constitutional authority, and assess their compatibility with congressional powers and legislation.¹⁴⁸ Justice Jackson describes three "tiers" of authority for presidential actions.¹⁴⁹ In the "first tier" are presidential actions taken "pursuant to an express or implied authorization

144. President Bush's Address does bear some resemblance to a loosely defined, somewhat obscure, class of presidential directives mentioned by Relyea, called "Presidential Announcements" and defined as "oral presidential directives . . . captured in an announcement which records what the President has prescribed or instructed." See Relyea, *supra* note 133, at 12. Yet, Relyea adds that Presidential Announcements "often are recorded in the *Weekly Compilation of Presidential Documents* However, they do not appear in the *Federal Register* or in the *Public Papers of the Presidents of the United States*." *Id.* President Bush's Address, while not published in the *Federal Register*, was published in the *Public Papers of the Presidents of the United States*, and thus falls outside the definition of this type of presidential directive.

It is interesting to note that a similar conclusion could also be drawn with respect to President Clinton's 1993 Embryo Decision, which was titled "Statement on Federal Funding of Research on Human Embryos" and was never published in the *Federal Register* but rather only in the *Weekly Compilation of Presidential Documents* and in the *Public Papers of the Presidents of the United States*. See *supra* note 60; see also President William J. Clinton, Statement on Federal Funding of Research on Human Embryos, 2 PUB. PAPERS 2142 (Dec. 2, 1994). Hence, President Clinton's Embryo Decision may also be viewed as falling outside of any of the known types of presidential directives.

145. Such authority is sometimes mentioned in particular statutes or may be construed as implied from powers constitutionally or statutorily granted to the President. See Gaziano, *supra* note 134, at 271-72, 276.

146. Some analogize such a president, who makes unrestricted use of executive power, to a "regulatory policy czar" or even to a king. See Cynthia R. Farina, *The "Chief Executive" and the Quiet Constitutional Revolution*, 49 ADMIN. L. REV. 179, 181 (1997); Branum, *supra* note 7, at 1, 33.

147. 343 U.S. 579 (1952).

148. *Id.* at 635-38 ("Presidential powers are not fixed but fluctuate, depending upon their disjunction or conjunction with those of Congress.").

149. *Id.*

of Congress,” in which the President’s authority “is at its maximum.”¹⁵⁰ The “second tier” includes presidential actions taken “in absence of either a congressional grant or denial of authority.”¹⁵¹ Finally, the “third tier” includes presidential actions that are “incompatible with the expressed or implied will of Congress,” in which the President’s power “is at its lowest ebb.”¹⁵² This Article begins its examination of the validity of President Bush’s Directive with a survey of the law governing the area of funding for scientific research in general and research involving hESCs in particular. Then, this Article classifies President Bush’s Directive and analyzes its validity under the appropriate “tier” offered in Justice Jackson’s *Youngstown* opinion (*Youngstown Analysis*).

1. *The Legal Framework of Federal Funding for Scientific Research*

Generally, the authority to fund biomedical research is granted to the Secretary of HHS, who acts through officers within NIH. The Public Health Service Act (PHSA) provides that “the Secretary is authorized to . . . make grants-in-aid to universities, hospitals, laboratories, and other public or private institutions, and to individuals for . . . research projects.”¹⁵³ Section 405 of the PHSA authorizes the Secretary, acting through the Directors of the NIH’s Research Institutes¹⁵⁴ to “encourage and support research, investigations, experiments, demonstrations, and studies in the health sciences.”¹⁵⁵ All funding decisions are subject to policies set by the Director of NIH, who is authorized to make such policies for the entire NIH.¹⁵⁶

Several statutes expressly affect the funding of human embryo research.¹⁵⁷ The most important is the Dickey Amendment. According to the Amendment:

None of the funds made available in [HHS Appropriations Acts] may be used for . . . the creation of a human embryo or embryos for research purposes . . . or . . . research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero.¹⁵⁸

150. *Id.* at 635.

151. *Id.* at 637.

152. *Id.*

153. 42 U.S.C. § 241(a)(3) (2000).

154. The NIH itself is an assemblage of individual research institutes, each of which charged with a particular area of research. *See id.* § 281.

155. *Id.* § 284(b)(1)(A).

156. *Id.* § 282(b)(1).

157. For instance, the NIHRA determines that “[t]he Secretary may conduct or support research on the transplantation of human fetal tissue for therapeutic purposes.” *See id.* § 289g-1(a)(1).

158. The Balanced Budget Downpayment Act, I, Pub. L. No. 104-99, § 128(2), 110 Stat. 26 (1996).

In light of the Rabb Opinion, which found that the NIH could fund research involving already-created hESC lines because such research would not qualify as the destruction of human embryos under the Dickey Amendment, it is widely accepted that the Dickey Amendment does not prohibit the funding of research that indirectly involves the destruction of human embryos (e.g., research involving stem cell lines created from destroyed embryos).¹⁵⁹ When read alongside each other, the Dickey Amendment and the PHSA authorize the Directors of the NIH's Research Institutes to support and conduct research involving hESCs so long as the research does not involve the creation of hESC lines or pose substantial risk to human embryos.

Most importantly, all funding for research conducted and supported by the NIH, including research involving embryos and hESCs, is also subject to the general instruction of § 101 of the NIHRA:

(b) Ethical review of research

(1) Procedures regarding withholding of funds

If research has been recommended for approval . . . the Secretary [of HHS] may not withhold funds for the research because of ethical considerations unless—

(A) the Secretary convenes an advisory board in accordance with paragraph (5) to study such considerations; and

(B)(i) the majority of the advisory board recommends that, because of such considerations, the Secretary withhold funds for the research; or

(ii) the majority of such board recommends that the Secretary not withhold funds for the research because of such considerations, but the Secretary finds . . . that the recommendation is arbitrary and capricious.

...

(3) Applicability

The limitation established in paragraph (1) . . . shall apply without regard to whether the withholding of funds on such basis is characterized as a disapproval, a moratorium, a prohibition, or other characterization.

...

159. See *supra* note 72 and accompanying text. Interestingly, by allowing for funding for research involving hESC lines (even if very few) President Bush's Directive seems to have accepted this premise. This position is also reflected in President Bush's op-ed piece, in which he explicitly stated that "[f]ederal funding for research on existing stem cell lines will move forward." See *President Bush's Op-Ed Piece*, *supra* note 104.

(5) Ethics advisory boards

(A) Any advisory board convened for purposes of paragraph (1) shall be known as an ethics advisory board . . .

(B)(i) An ethics board shall advise, consult with, and make recommendations to the Secretary regarding the ethics of the project of biomedical or behavioral research with respect to which the board has been convened.

(ii) . . . [T]he board shall submit to the Secretary . . . a report describing the findings of the board regarding the project of research involved and making a recommendation under clause (i) of whether the Secretary should or should not withhold funds for the project. . .

(C) An ethics board shall be composed of no fewer than 14, and no more than 20, individuals who are not officers or employees of the United States. The Secretary shall make appointments to the board from among individuals with special qualifications and competence to provide advice and recommendations regarding ethical matters in biomedical and behavioral research. Of the members of the board—

(i) no fewer than 1 shall be an attorney;

(ii) no fewer than 1 shall be an ethicist;

(iii) no fewer than 1 shall be a practicing physician;

(iv) no fewer than 1 shall be a theologian; and

(v) no fewer than one-third, and no more than one-half, shall be scientists with substantial accomplishments in biomedical or behavioral research.¹⁶⁰

The basis of this section was Congress's belief that "[c]ontinued progress in health research is seriously threatened by . . . administrative actions that undermine the peer review process at NIH and block research that holds promise for millions of Americans suffering from disease."¹⁶¹ Accordingly, § 101 was "intended to prohibit unilateral actions that block research approved by the merit review system"¹⁶² by forbidding "unreasonable prohibitions . . . imposed in an arbitrary manner on exceptional and promising research that have received approval by NIH's rigorous scientific, technical, and ethical review system"¹⁶³ and to "restore the freedom of inquiry essential to the continued success of the country's biomedical research."¹⁶⁴

160. 42 U.S.C. § 289a-1(b)(1)-(5).

161. S. REP. NO. 103-2, at 13 (1993).

162. *Id.* at 15.

163. *Id.* at 13.

164. *Id.* at 15.

To achieve these goals, § 101 establishes a “default” under which such funding for scientifically meritorious research should be granted unless it is duly withheld.¹⁶⁵ Furthermore, while the Secretary, acting through his subordinates, has authority to support and conduct research involving hESCs that meets the restrictions of the Dickey Amendment, § 101 takes away the Secretary’s authority to withhold funding from scientifically meritorious research involving hESCs because of ethical considerations without first receiving a recommendation to do so from an independent, duly-appointed Ethics Advisory Board. With this conclusion in mind, it is now possible to turn to the *Youngstown* Analysis of President Bush’s Directive.

2. *Classification of President Bush’s Directive Under Justice Jackson’s Taxonomy*

The question is now: under which of the “tiers” described by Justice Jackson does President Bush’s Directive fall? In order to fall under the “first tier,” a presidential action should rely on express or implied statutory authority.¹⁶⁶ If this had been the case, we could have expected that President Bush’s Address or the Fact Sheet would state the source of authority which they may have relied on,¹⁶⁷ yet neither of them does.¹⁶⁸ Therefore, we must determine whether President Bush’s Directive could have relied on such an express or implied authorization in legislation.

A survey of congressional legislation reveals that no statute explicitly grants the President the authority to decide the permissible object or means of scientific research in general or for purposes of funding in particular.

165. *Id.* at 20 (“It is the committee’s intent that . . . all research proposals that are approved by the merit review system and are awarded funding, and for which there is no justifiable reason for withholding or withdrawing funding, should be funded.”); *see also supra* note 48.

166. *See Youngstown Sheet & Tube Co. v. Sawyer*, 343 U.S. 579, 635 (1952) (Jackson, J., concurring) (noting that in such cases, the President’s power is at its maximum).

167. According to Branum, presidential directives normally state the source of their authority (whether legal or constitutional). In the rare case that a presidential directive totally disregards the issue of its authority, courts tend to question the validity of the presidential directive. *See Branum, supra* note 7, at 67-68.

168. Puzzlingly, no one has ever explicitly stated the source of President Bush’s authority to give his Directive and enforce it upon the NIH. The only reference I was able to find to the possible source of President Bush’s authority to give his Directive was by O. Carter Snead, the General Counsel of President Bush’s own Council on Bioethics. In an article dedicated entirely to President Bush’s Stem Cell Decision, Snead briefly mentioned that “the Bush policy demonstrates . . . a robust exercise of the *President’s authority as head of the executive branch* to allocate the appropriated funding according to the Administration’s priorities” (emphasis added). *See Snead, supra* note 73, at 498. Hence, according to Snead, the President’s source of authority to give his Directive was simply his being the “head of the Executive Branch.” As will be explained later in this section, this laconic explanation insinuates an “inherent” or “aggregate” constitutional presidential authority based on Article II of the Constitution. *See infra* Part II.B.3.

Hence, the question becomes whether President Bush's Directive relied on implied statutory authority.

Examining the statutes that regulate HHS and NIH funding of scientific research¹⁶⁹ reaffirms that the legislative language, on its face, does not lend itself to a construction implying that the President has the authority to intervene in the regulation of the funding for any type of scientific research, either inside or outside the context of research involving hESCs. Nevertheless, some scholars argue that there is more to the concept of implied presidential statutory authority.

The issue of implied presidential statutory authority is part of a lively debate regarding the measure of the President's control over the way executive officers carry out their statutorily-granted discretionary authorities and the President's power to affect the policies and decisions they make. This dispute is part of the longstanding and hotly debated controversy over the "unitary executive."¹⁷⁰ In this particular context, the debate revolves around the existence of a presidential takeover power—whether the President has the power to set policies and make decisions for executive agencies by "taking over" the duties bestowed upon them in legislation.¹⁷¹ One of the most prominent proponents of this "presidential takeover power" stemming from an implied presidential statutory authority is Dean Elana Kagan. According to Dean Kagan, the President has (and should have) the power to direct executive agencies by setting their policies and making decisions for them.¹⁷² Yet, unlike most proponents of the "unitary executive" theory, Dean Kagan does not find the source of the President's authority to take over the powers granted to agencies in the Constitution; rather, she reads legislation in a way that includes an implied presidential authority to take control of almost all of the legislative powers granted by Congress to particular agencies and executive officers.¹⁷³ Dean Kagan asserts that where a statute does not *explicitly exclude* the President

169. See generally 42 U.S.C. §§ 201-300ii-4 (2000).

170. For opposing views on the issue of the "unitary executive" and presidential powers to exert control over administrative agencies, see generally Yoo et al., *supra* note 7; Martin S. Flaherty, *The Most Dangerous Branch*, 105 YALE L.J. 1725 (1996). See also Elana Kagan, *Presidential Administration*, 114 HARV. L. REV. 2245, 2272-81 (2001). This dispute will be further discussed later in this section. See *infra* Part II.B.3.

171. For further discussion of this issue, see *infra* Part II.B.3.a.

172. See Kagan, *supra* note 170, at 2320, 2326-28 (noting that the President does not have authority to direct officials from independent agencies without the express grant of Congress).

173. *Id.* Kagan bases this construction of legislation on public policy reasons rather than on an historical reading of the Constitution. See *id.* at 2331-46.

from having the power to *possess* the discretionary authorities it grants to executive agencies, the statute should be construed to imply that the President has the power to use such authorities as his own.¹⁷⁴

Under Kagan's Doctrine, President Bush had the power to take over all of the authorities granted to the HHS and the NIH with respect to the funding of scientific research, including hESC research. Thus, to the extent that the HHS and the NIH had the authority to make a policy decision prohibiting the allocation of funding to research involving hESCs created after August 9, 2001, Kagan's Doctrine would assert that President Bush had the same authority and could have relied on this power in issuing his Directive.

However, even if we accept Dean Kagan's argument—which some scholars vehemently do not¹⁷⁵—President Bush's Directive could not have relied on this supposed implied statutory authority because NIHRA § 101 explicitly prevents HHS and the NIH from withholding funding for scientific research on ethical grounds without the prior recommendation of a duly appointed EAB.¹⁷⁶ Even if we espouse Kagan's Doctrine and presume that President Bush had all of the powers Congress granted to HHS and the NIH, he could still not have had a power that Congress did not grant to these agencies. In other words, since HHS and the NIH lack the authority to make decisions regarding the funding of scientific research based on ethical grounds without the prior approval of an EAB, so does President Bush.

We can surmise that President Bush's Directive could not have relied on an express or implied statutory authority, and thus does not fall within the boundaries of the “first tier” described in *Youngstown*. In addition, in light of the legislation regulating the funding of biomedical research¹⁷⁷—which indicates that Congress did not leave this area “an open field” for presidential action—we can determine that President Bush's Directive does

174. *Id.* at 2251. It is important to note that to date there seems to be no court decision implementing or even mentioning Dean Kagan's unitary executive theory (Kagan's Doctrine) or anything similar in analyzing presidential powers.

175. Some of the most convincing arguments against Kagan's Doctrine's basis and rationales are made by Kevin Stack. See Kevin M. Stack, *The President's Statutory Powers to Administer the Laws*, 106 COLUM. L. REV. 263 (2006). One of Stack's main arguments is that, contrary to Dean Kagan's assertions, Congress's practice of granting, in a handful of cases, legislative authorities to the President in name indicates that when Congress intends to grant the President legislative powers it does so explicitly and hence that her inference that wherever Congress did not do so indicates the existence of presidential powers goes not only against interpretation principles but also against common sense. See *id.* at 268, 276-99. Stack makes a compelling case against Kagan's Doctrine. His arguments and examples put the thesis promoted by Dean Kagan in a new light and substantially undermine the statutory construction that lies at the base of Kagan's Doctrine.

176. See 42 U.S.C. § 289a-1(b) (2000); see also *supra* Part II.B.1.

177. See *supra* Part II.B.1.

not fall under Justice Jackson's "second tier," which applies to presidential acts in the absence of a congressional grant or denial of authority.¹⁷⁸

Subsequently, and taking into consideration the language of NIHRA § 101—a language which explicitly seeks to *remove* from executive officers the power to make bioethical decisions with respect to the funding of research and requires them to have the bioethical issues properly deliberated in a highly visible public forum beforehand—President Bush's Directive seems to fall neatly under the definition of the "third tier" described in *Youngstown*. In giving his Directive, President Bush did exactly what Congress expressly sought to prohibit: in his capacity as the highest executive officer in the federal government, he made a decision to withhold funding for biomedical research involving hESCs. He did so based on his own moral and ethical beliefs, and without first receiving a recommendation to do so from an independent EAB, thus rendering his actions incompatible with § 101. Having reached this conclusion, this Article will now proceed to analyze the validity of President Bush's Directive under the premises of the "third tier."

3. *Analysis of the Validity of President Bush's Directive as Presidential Action Incompatible with the Expressed Will of Congress*

According to Justice Jackson:

When the President takes measures incompatible with the expressed or implied will of Congress, his power is at its lowest ebb, for then he can rely only upon his own constitutional powers minus any constitutional powers of Congress over the matter. Courts can sustain exclusive Presidential control in such a case only by disabling the Congress from acting upon the subject. Presidential claim to a power at once so conclusive and preclusive must be scrutinized with caution, for what is at stake is the equilibrium established by our constitutional system.¹⁷⁹

Following this "roadmap" for judicial review of presidential actions, we will assess the validity of President Bush's Directive by weighing the possible constitutional powers, which may have granted him the authority to give his Directive despite NIHRA § 101.

Lacking express constitutional language granting the President the authority to decide on matters involving scientific research and its funding, President Bush's Directive's only other possible source of authority is

178. See *Youngstown Sheet & Tube Co. v. Sawyer*, 343 U.S. 579, 637, 639 (1952) (Jackson, J., concurring) (explaining that "in absence of either a congressional grant or denial of [presidential] authority," Congress and the President have concurrent authority, which requires a more flexible examination than under either the "first tier" or the "third tier").

179. *Id.* at 637-38.

inherent presidential authority under the “Vesting Clause.”¹⁸⁰ In order to determine whether such inherent authority could have empowered President Bush to give his Directive, we need to answer the following two questions: (1) what is the measure of direction Presidents may exert over executive agencies and does the presidential power to direct executive agencies, which presumably stems from the President’s inherent authority, include the authority to set policies for agencies as President Bush did in his Directive; and (2) could inherent authority have empowered President Bush to “override” and act in variance with NIHRA § 101.

a. Inherent Presidential Authority and Its Applicability to President Bush’s Directive

“Inherent” or “aggregate” authority, as it has been referred to, is a somewhat controversial source of presidential constitutional power. The central proposition of the claim of inherent presidential constitutional authority is that under the auspices of the Vesting Clause,¹⁸¹ the President, as Chief Executive, is endowed with the power to direct the actions of executive agencies.

The controversy surrounding the existence of an inherent authority derives not only from its origin and undefined scope,¹⁸² but mostly from the fact that the Supreme Court has never explicitly acknowledged the existence of such authority.¹⁸³ This may be attributed, at least in part, to the

180. U.S. CONST. art. II, § 1, cl. 1 (“The executive Power shall be vested in a President of the United States of America.”).

181. *Id.*

182. See PHILLIP J. COOPER, BY ORDER OF THE PRESIDENT: THE USE AND ABUSE OF EXECUTIVE DIRECT ACTION, 4-5 (2002) (discussing the origins of “inherent authority”). Similar and even stricter words may be found in Justice Jackson’s concurring opinion in *Youngstown*:

Loose and irresponsible use of adjectives colors all non-legal and much legal discussion of presidential powers. “Inherent” powers, “implied” powers, “incidental” powers, “plenary” powers, “war” powers and “emergency” powers are used, often interchangeably and without fixed or ascertainable meanings.

The vagueness and generality of the clauses that set forth presidential powers afford a plausible basis for pressures within and without an administration for presidential action beyond that supported by those whose responsibility it is to defend his actions in court. . . . While it is not surprising that counsel should grasp support from such unadjudicated claims of power, a judge cannot accept self-serving press statements of the attorney for one of the interested parties as authority in answering a constitutional question But prudence has counseled that actual reliance on such nebulous claims stop short of provoking a judicial test. See *Youngstown*, 343 U.S. at 646-47 (Jackson, J., concurring).

183. The Supreme Court has referred to the concept of inherent presidential authority on numerous occasions, but the author is unaware of any case in which the Supreme Court has ever actually acknowledged the existence of an inherent authority in the President as a source of presidential power in a matter before the court. See, e.g., *Hamdi v. Rumsfeld*, 542 U.S. 507, 516-17 (2004); *id.* at 552 (Souter J., concurring in part, dissenting in part, and concurring in the judgment); *Loving v. United States*, 517 U.S. 748, 773 (1996); see also *Branum*, *supra* note 7, at 68; *George v. Ishimaru*, 849 F. Supp. 68, 71-73 (D.D.C. 1994).

fact that the language of inherent authority only surfaces when it is clear that the President does not have any other identifiable source of authority from which his acts may draw legitimacy.¹⁸⁴

Nonetheless, in light of the frequent invocation of inherent authority arguments by the Government—especially by the Clinton and Bush Administrations¹⁸⁵—and for the sake of completeness of the analysis of President Bush’s Directive, this Article assumes that inherent authority is as valid a source of presidential power as these Administrations have held it out to be. Thus, this part of the analysis assumes that, hypothetically, President Bush could have established his Directive on his Article II power to direct administrative agencies’ actions and policies.¹⁸⁶

(“This court rejects the argument that the President has ‘inherent’ appointment authority under the Take Care Clause of Article II of the Constitution to appoint persons to positions like this one. . . . No court has ever recognized that the President has such inherent authority. . . . The important work of the Commission on Civil Rights should not be impeded by continuing to argue about “inherent” Presidential power which no court in the nation’s history has ever recognized.”).

184. Henry Monaghan captured the essence of this phenomenon:

[W]hen . . . no readily identifiable legislative warrant exists, and arguably the President is implementing presidential policy alone, a different constitutional vocabulary surfaces. The Vesting Clause, the Take Care Clause, the Presidential Oath to ‘preserve, protect and defend the constitution of the United States,’ and the Presidents ‘inherent,’ . . . or ‘aggregate’ powers are all invoked in defense of the President’s conduct Each of these terms is simply a different formulation of the fundamental claim that the President’s conduct is valid even though no statutory authority exists.

See Henry P. Monaghan, *The Protective Power of the Presidency*, 93 COLUM. L. REV. 1, 14 (1993).

185. See, e.g., *Doolin Sec. Sav. Bank, F.S.B. v. Office of Thrift Supervision*, 139 F.3d 203, 211 n.6 (D.C. Cir. 1998) (rejecting an inherent power argument made by the Clinton Administration); *Ishimaru*, 849 F. Supp. at 71-72 (rejecting the argument that the President has “inherent” appointment authority under Article II of the Constitution); *Hamdi*, 542 U.S. at 516-17 (avoiding the issue of inherent presidential authority by finding that Congress authorized the President to order the plaintiff’s detention); *ACLU v. NSA*, 438 F. Supp. 2d 754, 780-81 (E.D. Mich. 2006) (holding that the President, as Commander in Chief, did not have inherent power to authorize the NSA to intercept international telephone and internet communications without a warrant); see also Yoo et al., *supra* note 7, at 729-30 (“Support for the unitariness of the executive branch does not necessarily require supporting the broad claims of inherent executive authority advanced by the Bush Administration.”); Kagan, *supra* note 170, at 2320-21 (addressing “President Clinton’s repeated invocation of a vaguely defined ‘executive authority’ to direct administrative officials to adopt certain presidential policies”); Gaziano, *supra* note 134, at 281 (“Some of President Clinton’s claims of implied and inherent authority were outrageous.”).

186. Despite my approach to the concept of “inherent authority” in this part of the Article, it is my opinion that “inherent authority” is a superfluous and sometimes even dangerous concept that the courts must not allow to exist as a valid source of presidential authority. In most cases in which the government raises “inherent authority” arguments, the use of this concept is misleading and mistaken and the government actually means to argue that the authority for the presidential action was implied from one of the President’s express constitutional powers. (This type of mistake often occurs with relation to the President’s powers under the “Commander in Chief” Clause.) Yet, in other cases, as described by Monaghan, the government has been invoking “inherent authority” to bolster arguments that the President had the power to take certain actions unsanctioned by any other express or implied constitutional or statutory authority. See Monaghan, *supra* note 184, at 24-32

However, President Bush's Directive did much more than merely provide direction to the NIH with respect to the funding of research involving hESCs: it set its policies for it. Can the President do that? Does the scope of the President's inherent authority include the ability to set policies for executive agencies? As mentioned above, a lively dispute persists with respect to the extent of control the President may exert over administrative agencies' actions and the measure of his ability to direct their policies.

i. The Unitary Executive Debate over the Presidential Power to Direct Executive Agencies

Three schools of thought predominate the debate surrounding the President's power to control discretionary authorities granted to executive officers. The first school, which I will refer to as Constitutional Unitarianism, envisions the President as somewhat of a "super-executive" who may, under the Constitution, "take over" almost any responsibility assigned to any inferior officer,¹⁸⁷ including policymaking authorities, and act in their stead in his own capacity as President or, alternatively, nullify the actions of which he does not approve.¹⁸⁸ According to this school of thought, the "presidential takeover power" exists even when the authorizing statute explicitly grants a discretionary executive power to a particular officer.¹⁸⁹

The main rationale of Constitutional Unitarianism is that the Vesting Clause grants "executive power" solely and exclusively to the President, who is the source of the executive power in the Government and who merely delegates it to entities and officers that Congress has charged with tasks, whereas these entities and officers are otherwise powerless to act

(critiquing this approach). I believe that accepting the government's inherent authority arguments in such cases may be dangerous since it would ratify the existence of presidential powers beyond those granted to the President by the Constitution or in legislation and thus beyond the checks and balances set forth in our constitutional scheme and the framework of the Separation of Powers Doctrine. This type of authority resembles the kind of power that an autocrat would have, not a President of a democracy. See Branum, *supra* note 7, at 33.

187. The exception to this is quasi-judicial administrative functions, namely when an agency is required to make decisions which affect specific individuals in specific cases. See *Myers v. United States*, 272 U.S. 52, 135 (1926) (explaining that the President has no power to influence or control executive officers when they are acting in a quasi-judicial manner); *Portland Audubon Soc'y v. Endangered Species Comm.*, 984 F.2d 1534, 1546-48 (9th Cir. 1993) (acknowledging that "when an agency performs a quasi-judicial . . . function its independence must be protected" and that "[t]here is no presidential prerogative to influence quasi-judicial administrative agency proceeding").

188. See Yoo et al., *supra* note 7, at 607.

189. See Steven G. Calabresi & Saikrishna B. Prakash, *The President's Power to Execute the Laws*, 104 YALE L.J. 541, 595 (1994) ("Because the President alone has the constitutional power to execute federal law, it would seem to follow that, notwithstanding the text of any given statute, the President must be able to execute that statute.").

unless and until such presidential delegation takes place.¹⁹⁰ Therefore, according to Constitutional Unitarians, Congress simply cannot grant executive power to any entity that is beyond the reach of the President,¹⁹¹ who is vested with the residual power to do, essentially, “whatever remains to be done after the formal Article I lawmaking process is concluded.”¹⁹² Accordingly, under Constitutional Unitarianism, executive agencies are merely a means to “assist” the President in carrying out the duties of the Chief Executive.¹⁹³ Thus, under the Constitutional Unitarian theory, because President Bush himself was the source of the NIH’s authorities, he had the authority to make funding decisions and set funding policies for the NIH, as he did in his Directive, as well as to nullify the NIH’s previously promulgated Final Guidelines, which he did not approve of and which did not align with his Stem Cell Decision.

The second school of thought, which I will refer to as Non-Constitutional Unitarianism, believes, like Constitutional Unitarians, that the President has takeover powers as well as the power to nullify executive policies and actions. However, unlike Constitutional Unitarians who rely on originalist-historical arguments, Non-Constitutional Unitarians argue that the President ought to have such Powers as a matter of public policy and desirable constitutional interpretation.¹⁹⁴ For the purposes of the analysis of President Bush’s Directive, the Non-Constitutional Unitarian view is identical to that of the Constitutional Unitarian theory in the sense that it too would perceive President Bush’s Directive as properly relying on a presidential authority to set and nullify policies for executive agencies.

Finally, the third school of thought, which I will call Moderate Unitarianism, consists of those who believe that the President’s authorities to direct executive agencies do not and must not entail the power to set policies and make decisions for agencies and in their stead but merely allow the President to “stir them in the right direction” through various means.¹⁹⁵ Unlike the two previous schools of thought, Moderate Unitarians

190. See *id.* at 593 (“[T]he Executive Power Clause grants ‘the executive Power’ solely and exclusively to the President. . . . Until and unless the President delegates ‘the executive Power’ to . . . entities or officers, they are constitutionally disempowered from acting.”).

191. *Id.*

192. Farina, *supra* note 146, at 181 (emphasis omitted) (criticizing the Constitutional Unitarian approach).

193. Constitutional Unitarians believe that although the President is the one who has the executive power, the President obviously cannot fulfill all the tasks imposed by Congress upon executive agencies alone and thus enlists the assistance of executive officers. See Calabresi & Prakash, *supra* note 189, at 593-94, 597-98.

194. See Kagan, *supra* note 170; see also Lawrence Lessig & Cass R. Sunstein, *The President and the Administration*, 94 COLUM. L. REV. 1 (1994) (basing their support of a unitary executive on constitutional interpretation).

195. See Farina, *supra* note 146 (condemning what she referred to as “the cult of the Chief Executive”); Peter L. Strauss, *Presidential Rulemaking*, 72 CHI.-KENT L. REV. 965, 968 (1997) [hereinafter Strauss, *Presidential Rulemaking*] (arguing that President Clinton’s

perceive the President as more of a “manager” and view presidential power over executive agencies as stopping short of the ability to dictate policies for and instruct such agencies on how they should use their discretionary powers.¹⁹⁶ Under the Moderate Unitarian approach, agencies “have relationships with the President in which he is neither dominant nor powerless.”¹⁹⁷ Moderate Unitarians therefore contend that in matters involving substantive decisions, executive officers are required to resist attempts by the President to impose his opinions upon them.¹⁹⁸ In a nutshell: supervision and direction are acceptable and even welcome, but substitution is not.

The Moderate Unitarian contention most relevant to this Article is that in setting policies for agencies, the President undermines the Separation of Powers Doctrine by partaking in the agencies’ rulemaking function, thereby overstepping into the “quasi-legislative” dimension of agencies.¹⁹⁹

practice of “owning” administrative actions “insufficiently respects the tension inherent in the Constitution between Congress’s power . . . and the fact of a single chief executive”); Peter L. Strauss, *The Place of Agencies in Government: Separation of Powers and the Fourth Branch*, 84 COLUM. L. REV. 573 (1984) [hereinafter Strauss, *Separation of Powers and the Fourth Branch*] (proposing a framework for analysis of the relationship between the President and agencies that balances the need for presidential oversight of the agencies with congressional authority and role in government); see also Richard H. Pildes & Cass R. Sunstein, *Reinventing the Regulatory State*, 62 U. CHI. L. REV. 1, 25 (1995) (claiming that the President cannot make decisions for executive agencies if Congress previously allocated authority to the agencies). Moderate Unitarianism acknowledges that the President has (and should have) various means of influencing agencies, like the constitutional power to remove executive officers and appoint others in their stead (with the limited exception of independent commissions created by Congress) as well as numerous “procedural” authorities over agencies including the authority to provide information to agencies so as to promote coordination in matters touching upon national policies, the authority to require agencies’ response on policy concerns relevant to them, or even the authority to direct agencies to further consider certain perspectives on a certain policy issue. See Strauss, *Separation of Powers and the Fourth Branch*, *supra*, at 649-50. See generally Peter L. Strauss & Cass R. Sunstein, *The Role of the President and OMB in Informal Rulemaking*, 38 ADMIN. L. REV. 181 (1986).

196. For a discussion of policy issues as they relate to Constitutional and Non-Constitutional Unitarianism as opposed to Moderate Unitarianism, see generally Thomas O. McGarity, *Presidential Control of Regulatory Agency Decisionmaking*, 36 AM. U. L. REV. 443, 445-63 (1987).

197. Strauss, *Separation of Powers and the Fourth Branch*, *supra* note 195, at 583; see also Strauss, *Presidential Rulemaking*, *supra* note 195, at 981-84 (arguing that the President may inquire into the duties delegated to agencies as long as he understands that the final decisions regarding the duties belong to the agency).

198. See Strauss, *Presidential Rulemaking*, *supra* note 195, at 973 (“That means that it is [an executive officer’s] right, and in some cases it may be his obligation, to refuse the President’s direction, even if he realizes that his disappointed boss may immediately send him out of office.”).

199. See *id.* at 967-68 (finding that the President’s practice insufficiently respects the tension between Congress’s power and his own office, namely “between the legal and the political”); see also Kagan, *supra* note 170, at 2320 (“Congress indeed has delegated discretionary power, but only to specified executive branch officials; by assuming responsibility for this power, the President thus exceeds the appropriate bounds of his office.”).

In addition, Moderate Unitarians contend that the Executive Office of the President lacks the resources necessary for making decisions, which require expertise and are therefore better left to executive agencies and officers.²⁰⁰ Thus, under the Moderate Unitarian theory, President Bush was prohibited from setting policies regarding the funding of research involving hESCs for the NIH, could not have simply nullified the Final Guidelines' part regulating such research, and did not have the power to give a presidential directive to that effect.

ii. *The Unitary Executive Debate in Court—Which School of Thought Prevails?*

Courts seem to have never directly endorsed any of the above schools of thought.²⁰¹ Yet, in numerous cases involving issues pertaining to the “unitary executive” debate, the Supreme Court rejected the Constitutional Unitarian positions and leaned more toward the theory of Moderate Unitarianism. The most obvious example of this judicial inclination is the pair of presidential removal-power cases, *Myers v. United States*²⁰² and *Humphrey's Executor v. United States*.²⁰³ In both cases, the issue was the extent of the President's authority to remove executive officers, and in both cases, the Government, taking the Constitutional Unitarian stance, argued that the President had constitutional authority to remove any executive officer at will. In *Myers*, the Supreme Court found that the President has an almost unlimited removal power stemming from the Article II vested executive powers.²⁰⁴ But only nine years later, the Supreme Court in *Humphrey's Executor* ruled that Congress may restrict the President's

200. See Farina, *supra* note 146, at 185 (“[I]t is unrealistic to think that the President can supervise the entire regulatory enterprise in any comprehensive and meaningful way.”). Allowing presidential involvement in such decisions would obviously increase the political component in these decisions at the expense of the expertise component. The Moderate Unitarian stance is that in this politics/expertise tradeoff, we must not allow “politics” to completely take over “expertise,” which plays a vital role in many executive decisions.

201. See Kagan, *supra* note 170, at 2250, 2271, 2322 (asserting that “the courts never have recognized the legal power of the President to direct even removable officials as to the exercise of their delegated authority”); see also Stack, *supra* note 175, at 270 (mentioning that although the question of whether the President has directive authority when a statute grants power to an executive officer was already prevalent during the nineteenth century, it “has never been squarely addressed by the Supreme Court”).

202. 272 U.S. 52 (1926).

203. 295 U.S. 602 (1935).

204. *Myers*, 272 U.S. at 134-35. In *Myers*, the Supreme Court decided the constitutionality of a statute providing that certain postmasters could only be removed with the approval of the Senate. The Court ruled that the statute was unconstitutional due to its infringement upon the principle of separation of powers and thus upheld the President's removal of a postmaster without the approval of the Senate. However, it is important to note that the *Myers* Court acknowledged, though in dictum, that Congress may be able to limit the President's ability to direct executive officials. *Id.* at 135.

removal power, thus practically rejecting the Constitutional Unitarian contention that Article II, § 1 grants the President an almost unlimited power to run the executive branch as the President sees fit.²⁰⁵

Another example of the Supreme Court's rejection of the Constitutional Unitarian position is the seminal case of *Morrison v. Olson*.²⁰⁶ In *Morrison*, the Supreme Court was once again called on to decide the constitutionality of a statute, namely the Ethics in Government Act, which insulated the position of Special Prosecutor from the influence and control of the President. The Supreme Court held that the Act was constitutional and that the Attorney General, as the President's representative, lacked the power to remove the Special Prosecutor at will (i.e. without "good cause") or control the way in which the Special Prosecutor carried out those duties. By doing so, the Supreme Court once again acknowledged Congress's ability to insulate certain executive officers and functions from the control of the President, and basically declined to accept the Constitutional Unitarian argument regarding the exclusivity and scope of the President's reign over all that is executive.²⁰⁷

These cases may suggest the existence of a "judicial trend" in the Supreme Court towards Moderate Unitarianism in general.²⁰⁸ Notably, these cases lie at the base of the conventional scholarly view, which also seems to follow the Moderate Unitarian approach: that the President lacks the authority to set policies and make decisions for executive agencies and in their stead.²⁰⁹ However, it appears that a "judicial trend" and a scholarly

205. *Humphrey's Ex'r*, 295 U.S. at 629-32. The issue in *Humphrey's Executor* was similar to that in *Myers*. Once again the President sought to remove an executive officer, only this time the officer was a Federal Trade Commissioner and the Supreme Court had to decide whether Congress could limit the President's powers of removal as it did with respect to FTC Commissioners. The Supreme Court ruled that Congress's law "insulating" the FTC Commissioners from the removal powers of the President was constitutional. However, the Court distinguished this case from *Myers* by holding again that actual participation of Congress in the removal process would be unconstitutional.

206. 487 U.S. 654 (1988).

207. *See id.* at 693-96 ("It is undeniable that the Act reduces the amount of control or supervision that the Attorney General and, through him, the President exercises over . . . investigation and prosecution The Attorney General . . . does not determine the counsel's jurisdiction; and his power to remove a counsel is limited.").

208. A much earlier indication of this "trend" (and possibly one of its precursors) is dictum in the Supreme Court's decision in *Kendall v. United States*, which seems to advocate the Moderate Unitarian approach with respect to presidential takeover powers. 37 U.S. 524, 610 (1838).

209. *See Kagan, supra* note 170, at 2320, 2324. As Dean Kagan observed:

The conventional view in administrative law, in apparent accord with [*Myers* and *Humphrey's Executor*], holds that the President lacks the power to direct an agency official to take designated actions within the sphere of that official's delegated discretion. The President has no authority to act as the decisionmaker, either by resolving disputes in the OMB process or by issuing substantive directives. This is because Congress, under the removal precedents, can insulate administrative policymaking from the President, and Congress has exercised this power by

convention are not authoritative enough to provide us with an unequivocal determination regarding the President's power to set policies for executive agencies. Furthermore, any attempt to predict whether this Moderate Unitarian inclination of the Supreme Court—which appears to have existed when *Morrison* was decided about twenty years ago²¹⁰—will persist (especially in the realigned Roberts Court), should be taken with a grain of salt. Therefore, it appears that we remain without any conclusive answer regarding the existence of presidential takeover powers in general and their applicability to President Bush's Directive in particular.

Nonetheless, as before, for the sake of completeness of the analysis, this Article will make the assumption that setting a policy for the NIH was within the boundaries of President Bush's constitutional inherent authority. This is not to say that in the particular case of President Bush's Directive, he properly used this inherent authority or that he may set funding policies for the NIH as he did, but merely that in principle, it is assumed that he could have found the power to do so with the inherent authority arguably vested in him. Thus, it is now necessary to determine whether President Bush's presumable inherent authority (to set policies for the NIH) gave him the power to override NIHRA § 101.

b. Inherent Authority as a Power to Override NIHRA § 101

This Article will now return to the “third tier” framework laid out in *Youngstown* and use it to evaluate the validity of President Bush's actions. At the heart of this part of the discussion lies the question of whether President Bush's supposed inherent authority to set policies for the NIH enabled him to give his Directive in spite of the NIHRA's instruction that a recommendation from a duly-established EAB precede an administrative decision to withhold federal funding from scientific research on ethical grounds.

A longstanding Supreme Court rule prohibits the President from acting in variance with a clear and valid statutory instruction,²¹¹ even in a state of

delegating the relevant discretion to a specified agency official, rather than to the President.

Id. at 2323, 2325; see also Pildes & Sunstein, *supra* note 195, at 24 (“What we might call the conventional view relies on the following three points[:]. . . (c) the President has no authority to make the decision himself, at least if Congress has conferred the relevant authority on an agency head.”).

210. See *supra* notes 206-07 and accompanying text.

211. See *Little v. Barreme*, 6 U.S. (2 Cranch) 170, 177-78 (1804) (holding that the congressional statute was clear and that the President had no power to expand its scope); see also CONGRESSIONAL STUDY OF EXECUTIVE POWER, *supra* note 134, at 10; Pildes & Sunstein, *supra* note 195, at 24-25 (“[N]either the President nor the agency head may violate the law, and to that extent both must follow the substantive statutory standard, whatever their policy views may be.”).

emergency.²¹² Yet, in light of the fact that the presidential act in the matter before us claims reliance on an inherent constitutional power, the issue at hand is somewhat more intricate than that which came before the Court in *Little v. Barreme*, which set this precedent.

Using “third tier” terminology, we can say that in his Directive, President Bush “took a measure” that was clearly “incompatible with the expressed will of Congress,” as manifested in NIHRA § 101. Hence, President Bush’s power was “at its lowest ebb,” and he could only have relied on his Constitutional powers, which presumably consisted of the President’s inherent authority to direct executive agencies. Following Justice Jackson’s scheme, we should determine whether this presidential power supersedes Congress’s constitutional legislative power under Article I, §§ 1 and 18 to legislate the NIHRA. According to *Youngstown*, presidential measures incompatible with the will of Congress would only be upheld by the courts where the President can claim an *exclusive* power to act and where such claim has been “scrutinized with caution” by the court. In other words, courts would only uphold presidential acts that go against clear statutory instructions in cases where it is clear that the Constitution empowers the President to act exclusively and Congress has no business interfering.²¹³ But is funding for scientific research in general, or for research involving hESCs in particular, an area that the Constitution designates as exclusively within the realm of the President’s powers? The answer appears to be in the negative and so the conclusion of this *Youngstown* Analysis is that President Bush’s Directive could not have overridden the NIHRA, even if it did rely on an inherent presidential authority to set funding policies for the NIH.

Still, as convincing and widely quoted as Justice Jackson’s *Youngstown* opinion may be, it is only dicta, and is therefore not instructive, but rather suggestive, and so are the conclusions it yields. Nevertheless, several court decisions dealing with presidential acts that violated congressional statutes bolster our conclusion that President Bush’s Directive could not have overridden the NIHRA. These decisions indicate that Justice Jackson’s opinion in *Youngstown* is a true reflection of the law, of the way courts perceive presidential acts that transgress congressional legislation, and of the very narrow latitude they are willing to afford to such acts.

212. See *Youngstown Sheet & Tube Co. v. Sawyer*, 343 U.S. 579 (1952) (rejecting the argument that the President’s “inherent power” to take action in a state of emergency legitimized the seizure of the steel mills); see also Monaghan, *supra* note 184, at 24-32 (“Whether or not any president can live with it, the literary theory of ‘The executive Power’ recognizes no presidential license to disregard otherwise concededly applicable legislation, even in an emergency.”).

213. Examples of such cases may include the President’s powers to set foreign policies (not including the signing of treaties) and to act as Commander in Chief.

The first example is, appropriately, the *Youngstown* Court's own majority opinion, which examined the validity of an executive order that facilitated the governmental seizure of privately owned steel mills.²¹⁴ Indeed, the presidential directive in *Youngstown*, which, according to the Government, relied on the President's inherent authority,²¹⁵ did not directly violate any particular congressional statute. However, as the Court acknowledged, the executive order not only failed to comply with statutory requirements for governmental seizures,²¹⁶ but also strove to settle a labor dispute by using seizure—a method Congress had previously refused to adopt.²¹⁷ Hence, the presidential directive in *Youngstown*, which the court refused to uphold, was really an attempt by the President to circumvent Congress's will by ignoring the law in much the same way President Bush's Directive simply ignored NIHRA § 101 requirements and the congressional will behind it.

Furthermore, in analyzing the Government's claim of inherent constitutional authority to issue the executive order, the *Youngstown* Court ruled that:

In the framework of our Constitution, the President's power to see that the laws are faithfully executed refutes the idea that he is to be a lawmaker The President's order does not direct that a congressional policy be executed in a manner prescribed by Congress—it directs that a presidential policy be executed in a manner prescribed by the President.²¹⁸

Accordingly, the *Youngstown* Court upheld the District Court's injunction against the President's executive order.

This case demonstrates the Supreme Court's reluctance to uphold an executive order, which implemented a presidential policy that both contravened and was at the expense of congressional policy properly set in legislation.²¹⁹ Although the majority's opinion in *Youngstown* apparently

214. See *Youngstown*, 343 U.S. at 582-83.

215. See *id.* at 582-84 (noting that the Government asserted that “a strike disrupting steel production for even a brief period would so endanger the well-being and safety of the Nation that the President had ‘inherent power’ to do what he had done”).

216. See *id.* at 585-86 (“There are two statutes which do authorize the President to take both personal and real property under certain conditions. However, the Government admits that these conditions were not met and that the President's order was not rooted in either of the statutes.”).

217. See *id.* at 586 (“Moreover, the use of the seizure technique to solve labor disputes in order to prevent work stoppages was not only unauthorized by any congressional enactment; prior to this controversy, Congress had refused to adopt that method of settling labor disputes.”).

218. *Id.* at 587-88.

219. See *id.* at 588 (“The power of Congress to adopt such public policies as those proclaimed by the order is beyond question.”). As explained above, the congressional policy took shape in two forms: one, in two statutes regulating governmental taking of property, and two, in refusal to allow for taking as means of settling labor disputes.

would have perceived the presidential action there as falling within the boundaries of the “second tier,” it nonetheless reflects the general sentiment expressed in Justice Jackson’s opinion with respect to presidential actions that circumvent legislation.

Another testament to the validity of the insights encapsulated in Justice Jackson’s opinion and to their applicability to President Bush’s Directive may be found in two cases—*State Highway Commission of Missouri v. Volpe*²²⁰ and *Train v. City of New York*²²¹—both of which deal with the President’s power to set money spending policies where such policies go against positive statutory instruction to spend certain sums. Though these cases did not involve direct judicial review of presidential instruction of executive officers, in both cases, the courts acknowledged that the administrative act under review was the result of a presidential instruction to act in spite of federal legislation.²²² Subsequently, in both cases, the courts overruled the administrative acts that implemented the presidential instruction not to spend,²²³ thus once again indicating the courts’ aversion to presidential policies and acts that are in clear conflict with legislation. These cases are also a testament to the courts’ unwillingness to defer to presidential instruction of executive agencies to implement presidential policies in a manner blatantly inconsistent with the law. Applying *State Highway* and *Train v. City of New York* to President Bush’s Directive not only indicates that courts would not accept the Directive, but also that the courts would frown upon the NIH’s implementation of President Bush’s Stem Cell Decision.²²⁴

The D.C. Circuit’s decision in *Chamber of Commerce v. Reich*²²⁵—the second case ever in which a presidential executive order was overruled in its entirety²²⁶—is another example of the courts’ unwillingness to tolerate

220. 479 F.2d 1099 (8th Cir. 1973).

221. 420 U.S. 35 (1975).

222. In *State Highway*, the Eighth Circuit reviewed a decision by the Secretary of Transportation to defer his authority to allocate funds apportioned by Congress to highway development in Missouri due to a presidential policy to limit government expenditures to control the inflation. 479 F.2d at 1103, 1108. In *Train v. City of New York*, the Supreme Court reviewed a decision by the Environmental Protection Agency (EPA) not to allot the City of New York funds appropriated by Congress for development of water and sewage infrastructure, whereas the EPA’s decision was the result of a direct instruction by the President to limit the sums which were originally appropriated for this purpose. 420 U.S. at 40.

223. See *State Highway*, 479 F.2d at 1118 (enjoining the defendants from withholding authority to appropriate funds under the Federal Aid Highway Act in Missouri); *City of New York*, 420 U.S. at 44, 47 (finding that the letter from the President and the Administrator’s withholding of the funds could not “be squared with the statute”).

224. For a discussion of the NIH’s policy implementing President Bush’s Directive, see *infra* Part II.C.

225. 74 F.3d 1322 (D.C. Cir. 1996).

226. See Branum, *supra* note 7, at 38 (explaining that President Clinton was “only the second President to have an executive order struck down by the courts in its entirety”).

presidential actions intended to circumvent statutes. In *Reich*, the Government attempted to defend an executive order issued by President Clinton, which clearly contradicted a congressional act, by arguing that another later, though more general statute granted the President the authority to issue his order in abrogation of the former statute.²²⁷ The D.C. Circuit did not accept the Government's arguments and held that the earlier, more specific statute preempted President Clinton's executive order.²²⁸ Although the Court's reasoning in this matter seemed to involve mere statutory construction, its decision indicated the Court's reluctance to uphold a presidential action that stands in clear conflict with a valid statute.²²⁹

Lastly, the D.C. Circuit's decision in *Building & Construction v. Allbaugh*²³⁰ addressed the validity of an executive order issued by President George W. Bush that prohibited executive agencies entering into agreements with contractors from requiring or prohibiting the implementation of certain pro-union labor practices,²³¹ and which was presumably in conflict with the National Labor Relations Act (NLRA).²³² In its arguments during the trial, the Government contended that the President's authority to issue the executive order stemmed from his inherent constitutional power to direct executive agencies.²³³ The District Court did not accept the Government's arguments regarding the President's authority to issue the order, but rather found it to be "presidential lawmaking" a la *Youngstown*, and overruled the relevant part in the executive order as preempted by the NLRA.²³⁴ On appeal, the D.C. Circuit accepted the Government's argument that the President's authority to issue the executive order stemmed from his "supervisory authority over the Executive Branch"²³⁵ in an area of regulation that is not preempted by the

227. See *Reich*, 74 F.3d at 1332-33 (rejecting the argument that the Procurement Act of 1949 granted broad power to the President over the more specific National Labor Relations Act).

228. *Id.* at 1332-39.

229. See *id.* at 1338-39 (concluding that "the Executive Order is regulatory in nature and is pre-empted by the NLRA which guarantees the right to hire permanent replacements"); see also Gaziano, *supra* note 134, at 287 ("*Reich* stands for the seemingly obvious proposition that the President may not use his statutory discretion in one area to override a right or duty established in another law.").

230. 295 F.3d 28 (D.C. Cir. 2002).

231. Exec. Order No. 13,202, 66 Fed. Reg. 11,225 (Feb. 17, 2001).

232. National Labor Relations Act (NLRA), ch. 372, 49 Stat. 449 (1935) (codified at 29 U.S.C. §§ 151-169 (2000)); see *Bldg. & Constr. Trades Dep't v. Allbaugh*, 172 F. Supp. 2d 138, 162 (D.D.C. 2001) (making two sections of President Bush's executive order invalid because they were preempted by the NLRA).

233. See *Allbaugh*, 172 F. Supp. 2d at 159 ("Defendants' constitutional argument rests on the 'well-established' power . . . to supervise and guide subordinate executive officials to ensure the consistent execution of the laws.").

234. *Id.* at 172.

235. *Allbaugh*, 295 F.3d at 32-33.

NLRA,²³⁶ and thus overturned the District Court's decision and upheld the executive order.²³⁷ Yet, the important part of the D.C. Circuit's decision for our purposes is its reasoning. The D.C. Circuit did not base its decision on the premise that the President's inherent authority empowered him to act in variance with congressional statutes, but rather on the fact that the disputed segment in the executive order was preceded by the words "[t]o the extent permitted by law."²³⁸ In the eyes of the D.C. Circuit, the prefix "to the extent permitted by law" was assurance enough that "if [an agency implementing the executive order] is prohibited, by statute or other law, from implementing the Executive Order, then the Executive Order itself instructs the agency to follow the law."²³⁹ In fact, the D.C. Circuit found the redeeming qualities of this prefix so great that had the presidential directive in *Youngstown* been supplemented with this qualification, the court opined that it would have made most of the discussion regarding its validity moot.²⁴⁰ *Building & Construction* therefore demonstrates once more the courts' view that presidential actions are permissible and will be tolerated only to the extent they do not contravene valid congressional legislation.

The aforementioned cases indicate that Justice Jackson's opinion is a true crystallization of how courts perceive and rule in matters involving presidential actions that run against valid statutory instruction. Evidently, courts tend to be suspicious of presidential directives that do not comport with legislation, and they tend not to uphold such directives or their progeny.²⁴¹ The conclusion to be drawn from the above is that Justice

236. *Id.* at 34.

237. *Id.* at 36.

238. *Id.* at 33.

239. *Id.*

240. *Id.* Thus, it appears that according to the D.C. Circuit, if all presidential directives had the prefix "to the extent permitted by law" there would never be questions regarding their legality or validity. As a side note, I find it worth adding that I believe the D.C. Circuit was wrong in its decision that practically allows the President to leave the legal inquiry about the legality of his executive orders' instructions to agencies and expect them to find what is "permitted by law" and what is not. Turning the phrase "to the extent permitted by law" into a "kosher stamp" for just any presidential directive—outrageous and outright illegal as it may be—might encourage the President to issue directives of dubious legality which might eventually be enforced by executive officers who wish to avoid direct confrontations with the President. This clearly undesirable situation cannot simply be cured via semantic maneuvers.

241. Notably, an even broader possible implication of these cases is that courts would not hastily acknowledge and enforce a presidential claim of authority that has no, or hardly any checks on it, especially as Justice Jackson says, when such a right is in direct contradiction of the legitimate use of constitutional authority by another branch of the government (e.g., Congress's Article I authority to legislate the NIHRA). See *Youngstown Sheet & Tube Co. v. Sawyer*, 343 U.S. 579, 637-38 (1952). The *Youngstown* decision and the majority opinion in *Morrison* both support this proposition. According to the *Morrison* Court, the President's powers may not be construed to be entirely separate or detached from the powers granted to the other branches of government. *Morrison v. Olson*, 487 U.S. 654,

Jackson's opinion may well be viewed as the judicial standard—or blueprint for such a standard—that courts would apply in cases of presidential claims of inherent authority to instruct executive agencies to take action in contravention of legislation. Application of this standard would mean that inherent authority may not serve the President as a power to override federal statutes in general, and that to the extent that President Bush relied on such an authority in giving his Directive, it could not have enabled him to give his Directive in contradiction to the NIHRA.

Having found that inherent authority—despite the permissive assumptions made here regarding its existence and expansive scope—could not have empowered President Bush to give his Directive in contravention to the NIHRA, and with the lack of any other source of authority that President Bush's Directive could have relied on, we must determine that the Directive is illegal, and thus invalid.

C. The NIH's Actions Examined

The immediate implication of President Bush's Directive's invalidity is that it did not, and does not carry any authority over executive agencies. However, prior to discussing the implications of its illegality in more detail, there is merit in an examination of the measures taken by the NIH following President Bush's Address and their legality.

Professor Peter Strauss once wrote that “[i]t is far easier [for an executive officer] to act as a servant, than as an independent authority under instructions from one's principal.”²⁴² This epigram seems to concisely capture the NIH's response to President Bush's Directive. On the day President Bush gave his Address, Dr. Ruth Kirschstein, the Acting Director of the NIH at that time, subordinated her discretion²⁴³ and the

693-94 (1988). In other words, the *Morrison* Court opined that the President's actions do not occur in a “vacuum,” but rather are in constant interaction with other powers that exist within the Government—powers which the President's actions must reckon with. See also William J. Olson & Alan Woll, *Executive Orders and National Emergencies: How Presidents Have Come to “Run the Country” by Usurping Legislative Power*, 358 CATO INST. POLICY ANALYSIS 8-10 (1999) (“The Court's preference for constitutionally enacted laws over presidential directives not clearly based on constitutional or statutory authority is evident from its treatment of the implementation of regulations promulgated under such directives.”).

242. Strauss, *Presidential Rulemaking*, *supra* note 195, at 974.

243. Under 42 U.S.C. § 282(b)(1), the Director of NIH has the authority to set policies for the entire NIH. For further discussion of this policymaking authority, see *supra* Part II.B.1.

discretion of the Directors of the NIH's Research Institutes²⁴⁴ to that of the President by immediately and unreservedly endorsing President Bush's Stem Cell Decision.²⁴⁵

A Moderate Unitarian scrutiny of the NIH's actions following President Bush's Directive implicates that the NIH's actions amounted to unjustified obsequiousness towards the President, which is not only repugnant to principles of proper administration, but is also illegal. According to Moderate Unitarianism, regardless of NIHRA § 101, the NIH's Acting Director had an obligation to not simply accept President Bush's imposition of his own personal policy upon the NIH, even if that would have meant that she might risk her office.²⁴⁶ Rather, Dr. Kirschstein, as an acting head of an agency, was duty bound to use her autonomous discretion. She ought to have seriously considered the President's stance on the issue of research involving hESCs²⁴⁷ (and was indeed under a constitutional obligation to do so), but nonetheless eventually make the decision by herself and with the best interests of the public in mind rather than the personal sentiments of the President. Thus, under a Moderate Unitarian approach, the submissiveness of the NIH and its Acting Director constituted an illegal substitution of their own discretion with that of the President. Moreover, under Moderate Unitarian theory, the NIH's actions amounted to abandonment of its public stewardship and statutory charge, which are meant to serve as an important check on the President's executive authority from becoming all-inclusive and all-reaching.²⁴⁸ In simpler terms, the Moderate Unitarian approach would hold that the NIH forsook its duties and acted as the President's lackey, thus allowing the President's beliefs to become the law of the land. Hence, under the Moderate Unitarian approach, the NIH's actions pursuant to President Bush's Directive constituted a capricious executive decision and an abuse of the NIH's discretion to make its own research funding decisions, such that a court should set them aside.²⁴⁹

244. Under 42 U.S.C. § 284(b)(1), the Secretary, acting through the Directors of the NIH's research institutes, may grant funding for scientific research.

245. See Kirschstein Statement, *supra* note 4. For a detailed discussion of the actions taken by the NIH to implement President Bush's Directive, see *supra* Part I.C.

246. See *supra* text accompanying note 198.

247. See Stack, *supra* note 175, at 314 (stating that executive officials are subject to "an obligation to carefully consider the President's position[s]").

248. See *id.* at 316 ("[T]he mere possibility of resistance [by executive officials to the President's preferred construction or use of a statute] creates a legal check on presidential abuse internal to the executive branch. . . .").

249. See 5 U.S.C. § 706(2)(A) (2000) (directing reviewing courts to hold unlawful and set aside actions that are "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law"). For further discussion of this possible cause of action, see *infra* Part III.D.

However, it appears that Dr. Kirschstein's NIH did not share the Moderate Unitarian viewpoint. In what seems to be the NIH's only explanation for its unqualified acceptance of President Bush's Directive, the NIH proclaims on its website:

As the head of the executive branch of the federal government, which includes the National Institutes of Health, the President of the United States has the final responsibility and authority to set federal government policy for funding human embryonic stem cell research. But Congress has appropriations authority and can possibly override the President's decision.²⁵⁰

Indeed, this is a true statement of the Constitutional Unitarian view. And yet, even under a Constitutional Unitarian approach, the NIH's actions were clearly illegal.

First and foremost, regardless of President Bush's authority to give his Directive, the Directors of the NIH Research Institutes and its Acting Director (NIH Officers) were still bound to follow the numerous requirements of NIHRA § 101,²⁵¹ including the requirement that, before they impose a moratorium on certain kinds of scientific research (e.g., involving hESCs produced after August 9, 2001 at 9:00 p.m.), they must receive a recommendation to do so from a duly-established Ethics Advisory Board.²⁵² Having not fulfilled this requirement, the NIH Officers' actions pursuant to President Bush's Directive were in excess of the Officers' statutory authority, and thus illegal.²⁵³

Moreover, the NIH's announcement of its withdrawal of the Final Guidelines' part relating to research involving hESCs (the Repeal) constitutes in and of itself an illegal action under the Administrative Procedure Act. Since the Final Guidelines came under the definition of a

250. NIH FAQs, *supra* note 15.

251. See *supra* Part II.B.1. It is worth noting that both the NIH's Research Institutes Directors' authority to fund scientific research under 42 U.S.C. § 284(b)(1) and the NIH Director's authority to make general policies for the entire NIH under 42 U.S.C. § 282(b)(1) stem from the power of the Secretary. Specifically, both sections state that the duties and authorities they grant are actually the Secretary's, who is acting *through* his subordinates, the NIH Officers. Hence, to the extent that the funding granting authority in 42 U.S.C. § 284 and the policymaking authority in 42 U.S.C. § 282(b)(1) are being used by the NIH Officers, these Officers are duty-bound by limitations imposed on the source of their own authority, namely the Secretary, such as those enumerated in the NIHRA § 101. This proposition is also supported by the principle that a principal may not delegate powers greater than the powers she possesses herself. Thus, a delegate cannot possibly have more power than the principal could have delegated to her and the NIH Officers could not have ignored the NIHRA § 101 simply because it is addressed to the Secretary.

252. 42 U.S.C. § 289a-1(b) (2000).

253. It is also worth mentioning in the context of the grants' allocation proceedings, which the NIH Officers failed to follow, that although there is no question that the NIH Officers had ample discretion in making funding decisions with respect to particular kinds of research or a particular research project, they did not have such discretion with respect whether or not *to consider* the allocation of such funding to begin with.

“rule”²⁵⁴ in the APA and were not exempt from its notice and comment requirements,²⁵⁵ their promulgation and repeal were subject to these requirements.²⁵⁶ These requirements dictate that prior to repealing the Final Guidelines or a part thereof, the NIH was under an obligation to publish a general notice in the Federal Register about its intention to repeal the Guidelines, provide interested parties an opportunity to comment on the planned repeal, consider the comments and the relevant matters presented, and only then use its discretion to make an informed decision about repealing the Guidelines.²⁵⁷ The NIH indeed published a notice in the Federal Register announcing the Repeal.²⁵⁸ Yet, it did not provide interested parties the opportunity to comment on the planned Repeal and subsequently, did not weigh any opposition prior to the Repeal. Rather, the announcement unilaterally imposed the restrictions in violation of the APA’s notice and comment requirements²⁵⁹ (which, as mentioned earlier, HHS undertook to follow²⁶⁰). It appears that the NIH attempted to justify these omissions by arguing that President Bush’s Directive made compliance with these requirements unnecessary, thus invoking the “good cause” exception to the notice and comment requirements.²⁶¹ Specifically, in its withdrawal notice, the NIH stated that “[t]he President has determined the criteria that allow Federal funding for research using existing embryonic stem cell lines Thus, the [Final] Guidelines as they relate to [hESC] derived from human embryos are no longer needed.”²⁶² Nonetheless, although HHS’s undertaking to follow the notice and comment requirements does not apply to cases where the “good cause” exception is applicable,²⁶³ it is doubtful whether courts would accept this explanation as justification for the NIH’s noncompliance with the APA’s notice and comment requirements. According to several Courts of Appeals’ decisions, the “good cause” exception would not only be narrowly construed, but would also apply only in a limited set of

254. The Final Guidelines fell under the definition of a “rule” under 5 U.S.C. § 551(4), and therefore, their repeal was considered “rulemaking” under 5 U.S.C. § 551(5).

255. See *supra* note 83.

256. 5 U.S.C. § 553 (2000); see also *Consumer Energy Council of Am. v. FERC*, 673 F.2d 425, 446 (D.C. Cir. 1982); *Env’tl. Def. Fund, Inc. v. Gorsuch*, 713 F.2d 802, 816 (D.C. Cir. 1983); *Natural Res. Def. Council, Inc. v. EPA*, 683 F.2d 752, 761-65 (3d Cir. 1982).

257. 5 U.S.C. § 553(c).

258. *National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells*, 66 Fed. Reg. 57,107 (Nov. 14, 2001).

259. *Id.*

260. See *supra* note 83.

261. 5 U.S.C. § 553(b)(B).

262. *Guidelines for Research Using Stem Cells*, 66 Fed. Reg. at 57,107.

263. Because the HHS’s undertaking involves only matters of grants and benefits, it does not necessarily apply to matters coming under the premise of 5 U.S.C. § 553(b), i.e., “when the agency for good cause finds . . . that notice and public procedure thereon are impracticable, unnecessary, or contrary to the public interest.” 5 U.S.C. § 553(b)(B).

circumstances that do not exist in this case.²⁶⁴ Hence, it seems that the NIH's explanation of its noncompliance with the APA's notice and comment requirements was not sufficient to exempt it from these requirements, and the Repeal was illegal under the APA.

An interesting question that arises in this context is whether President Bush's Directive was authoritative enough to enable the NIH to simply disregard the APA's instructions. In other words, could the President have lawfully given the NIH instructions and empowered it to act in violation of the APA? Following the Supreme Court's reasoning in *Franklin v. Massachusetts*,²⁶⁵ it may be argued that, just like presidential actions are not reviewable under the APA out of "respect for the separation of powers and the unique constitutional position of the President,"²⁶⁶ agency actions that follow and implement such presidential actions may be exempt from the APA.²⁶⁷ Applying this proposition to the matter at hand would result in the conclusion that since President Bush's Directive's disregard of the APA's notice and comment requirements is not reviewable under the APA, so too are the pursuant actions taken by the NIH to implement the Directive. However, even if we assume that President Bush's Directive's violation of the APA would be deemed non-reviewable under the APA,²⁶⁸

264. According to 5 U.S.C. § 553(b)(B), there are three grounds for finding "good cause," namely when "notice and comment" would be "impracticable, unnecessary, or contrary to the public interest." 5 U.S.C. § 553(b)(B). "Impracticability" is interpreted as applicable in cases of emergency. *Am. Fed'n Gov't Emp. v. Block*, 655 F.2d 1153, 1156 (D.C. Cir. 1981) (limiting use of the good cause exceptions to "emergency situations"). However, no such emergency existed in the matter of President Bush's Directive, and so it is unlikely that courts would accept a "good cause" for emergency argument. *See* *Consumer Energy Council of Am. v. FERC*, 673 F.2d 425, 447-48 (D.C. Cir. 1982) (holding that an emergency does not exist when an agency finds regulations to be defective); *see also* *Env'tl. Def. Fund, Inc. v. EPA*, 716 F.2d 915, 920 (D.C. Cir. 1983); *Natural Res. Def. Council, Inc. v. EPA*, 683 F.2d 752, 764 (3d Cir. 1982). As for non-necessity, according to the D.C. Circuit, this ground would have applied only had the Repeal been a "routine determination, insignificant in nature and impact and inconsequential to the industry and to the public." *See* *Util. Solid Waste Activities Group v. EPA*, 236 F.3d 749, 755 (D.C. Cir. 2000) (quoting *South Carolina v. Block*, 558 F. Supp. 1004, 1016 (D.S.C. 1983)). Since the Repeal is anything but "routine," "insignificant in nature and impact," and is consequential to the industry and the public, this ground too, would not be available to the NIH in attempting to rely on the "good cause" exception. And as for the "public interest" ground for the "good cause" exception, according to the D.C. Circuit it would only apply when "the interest of the public would be defeated by any requirement of advance notice." *Id.* at 755 (quoting *United States Department of Justice, Attorney General's Manual on the Administrative Procedure Act* 31 (1947)). As before, it is hard to see how following the notice and comment requirements in this case would defeat the public's interest, and so we should surmise that none of the grounds enumerated in 5 U.S.C. § 553(b)(B) are applicable to the Repeal and thus that the NIH could not have relied on them.

265. 505 U.S. 788 (1992).

266. *Id.* at 800-01.

267. In so doing, courts following *Franklin* would actually accept a narrow set of circumstances in which the President may act in violation of the APA.

268. Opposing this proposition is the aforementioned courts' intolerance of presidential actions that may contradict valid law. *See supra* Part II.B.3.

this conclusion seems to be far-fetched with respect to the NIH. The APA is unequivocal about its applicability to agency actions.²⁶⁹ Despite the *Franklin* Court's holding that applying the APA to the President would require an express statement by Congress to this effect,²⁷⁰ Congress has made it clear that the APA applies to executive agencies. Therefore, it is highly unlikely that courts would require a further "statement of applicability" of the APA to executive actions, including actions that are the direct result of presidential directives. In other words, even if we accept the proposition that presidential actions may legitimately run in the face of the APA, it does not follow that agencies may wield *Franklin* as a shield against judicial review when they are acting under such Presidential instructions.²⁷¹ Hence, the NIH could not have used President Bush's Directive as a justification for its disregard of the APA's notice and comment requirements.

III. THE IMPLICATIONS OF THE ILLEGALITY OF PRESIDENT BUSH'S DIRECTIVE AND OF THE ENSUING ACTIONS TAKEN BY THE NIH

The severity of the findings reached in the previous Part—that President Bush's Directive lacked authority and that the NIH's implementation of his Directive was blatantly illegal (the Contestable Actions)—is undeniable and invites a judicial challenge. This Part will discuss some possible challenges that the Contestable Actions may face and enumerate some legal remedies called for by such challenges. But, prior to discussing such challenges, it is important to address the preliminary issue of standing.

One would assume that scientists seeking to secure federal funding for scientifically meritorious research proposals²⁷² involving hESC lines created after August 9, 2001, or otherwise not in compliance with President Bush's Stem Cell Decision would have standing. Such scientists would

269. See 5 U.S.C. § 551(1) (2000) ("[A]gency' means each authority of the Government of the United States, whether or not it is within or subject to review by another agency. . . .").

270. *Franklin*, 505 U.S. at 801.

271. Such a situation not only runs against the basic principle that agency action must be based on legal mandate, but also goes directly against the Separation of Powers Doctrine and the important principle of checks and balances since it proposes a sphere in which a President may be allowed to act and authorize actions that go against the law without such actions being subject to judicial review. It is most improbable that courts would seriously consider such a proposition.

272. It may be argued that scientific merit and allocation of funding thereof is a matter "committed to agency discretion by law" under 5 U.S.C. § 701(a)(2), and therefore, not subject to judicial review. See *Lincoln v. Vigil*, 508 U.S. 182, 192-94 (1993). However, the arguments possibly raised by scientist-plaintiffs with respect to the Contestable Actions would not involve the non-allocation of research funds by the NIH for hESC research, but rather the actions taken by the NIH with respect to the repeal of the mechanism that would have allowed for the allocation of such funding. Hence, 5 U.S.C. § 702(a)(2) should not be a justiciability barrier in the matter at hand.

probably not have a particular hardship establishing that their claims fall within the “zone of interests”²⁷³ under the APA²⁷⁴ as well as under the NIHRA.²⁷⁵ However, a question may arise with respect to such scientists’ ability to show that the Contestable Actions have caused them an injury-in-fact²⁷⁶ and that they have a personal stake in the lawsuit’s outcome.²⁷⁷ Presumably, since there is no certainty that such scientists would have been able to secure discretionary funds from the NIH to support their hESC research had the Final Guidelines been in place, it is unclear whether they may be able to convince a court that they have been injured by the Contestable Actions and therefore, have a personal stake in overturning them.

Nevertheless, it is unlikely that the issue of injury-in-fact and stake in the outcome of the proceedings would bar scientists whose research involves hESCs from establishing that they would have standing. First, the Supreme Court has held in cases involving a hardship posed by the government to obtain a benefit, that it is not necessary for the plaintiff to prove that she would have obtained the benefit “but for the hardship” in order to establish standing. Rather she must show only that she is able and ready to apply for the benefit and that the governmental policy is preventing her from doing so.²⁷⁸ Second, the Supreme Court has held on more than one occasion that the injury-in-fact requirement may be satisfied not only by demonstrating an economic injury, but that an injury may be of other kinds.²⁷⁹ For example, a group of hESC researchers could claim that their

273. See *Ass’n of Data Processing Serv. Orgs., Inc. v. Camp*, 397 U.S. 150, 153, 156 (1970); see also *Clarke v. Sec. Indus. Ass’n*, 479 U.S. 388, 399-400 (1987) (discussing the “zone of interests” test).

274. 5 U.S.C. § 702 (2000); see also *Data Processing*, 397 U.S. at 154 (“Where statutes are concerned, the trend is toward enlargement of the class of people who may protest administrative action.”).

275. 42 U.S.C. § 289a-1 (2000).

276. See *Data Processing*, 397 U.S. at 152 (“The first question is whether the plaintiff alleges that the challenged action has caused him injury in fact, economic or otherwise.”).

277. See JOHN E. NOWAK & RONALD D. ROTUNDA, *CONSTITUTIONAL LAW*, § 2.12(f)(2), 91 (7th ed. 2004) (“Whether a party has ‘alleged such a personal stake in the outcome of the controversy as to assure that concrete adverseness which sharpens the presentation of issues’ is, we are told, ‘the gist’ of the question of standing.”).

278. *Id.*; see, e.g., *N.E. Fla. Chapter of the Associated Gen. Contractors of Am. v. Jacksonville*, 508 U.S. 656, 666 (1993). Notably, this case involved an equal protection matter and the injury-in-fact element therein was “the [plaintiffs’] inability to compete on an equal footing in the bidding process, not the loss of a contract.” *Id.* Similarly, it may be argued that in the matter at hand the scientist-plaintiffs’ injury-in-fact has been their inability to apply for federal funding for research involving hESCs not in accordance with President Bush’s Directive rather than the loss of the funds themselves.

279. See, e.g., *Data Processing*, 397 U.S. at 154 (“That interest, at times, may reflect ‘aesthetic, conservational, and recreational’ as well as economic values.” (quoting *Scenic Hudson Preservation Conf. v. FPC*, 354 F.2d 608, 616 (2d Cir. 1965))); *United States v. Students Challenging Regulatory Agency Procedures (SCRAP)*, 412 U.S. 669, 686-89 (1973) (granting standing where aggrieved party claimed injury due to diminished use and enjoyment of local natural resources).

injury relates to their interest in the advancement of science as it pertains to hESC research, which is hindered by the impediments to scientific progress put in place by the Contestable Actions. Similarly, they may argue that their injury relates to an interest they have as biomedical researchers in the harm caused to the public's health by the impediments on advancement of stem cell based therapies placed by the Contestable Actions. It therefore appears that researchers partaking in research involving hESCs may arguably have standing to challenge the Contestable Actions.

A. Challenging President Bush's Directive

A challenge to President Bush's Directive is likely to be based on the argument that it essentially constitutes forbidden presidential lawmaking. President Bush's and the NIH's emphasis that the Directive is "*the President's policy*"²⁸⁰ bolsters this argument. Furthermore, the fact that the Directive runs against the explicit instructions of the NIHRA makes it all the more clear that President Bush's Directive "does not direct that a congressional policy be executed in a manner prescribed by Congress—it directs that a presidential policy be executed in a manner prescribed by the President."²⁸¹

The basic premise of this challenge is that allowing President Bush's Directive to persist despite its clear undermining of a constitutionally valid congressional statute would legitimize the usurpation of legislative authority by presidents.²⁸² Furthermore, in issuing his Directive, despite his likely awareness of his lack of authority to promote *his* policy (i.e., his Stem Cell Decision),²⁸³ President Bush's actions run against one of most basic understandings about the nature of the Government of the United States, namely that it is "a government of laws, and not of men."²⁸⁴ Thus, courts would likely find that President Bush's Directive is in clear violation of the Doctrine of Separation of Powers and strike it down in its entirety, despite their basic reluctance to revoke presidential directives.²⁸⁵

"But He [the Democratic President] Started It"

A popular defense argument among Presidents whose actions are challenged is that their actions did not go beyond prior unchallenged

280. See *supra* Part I.C, notes 102-05 and accompanying text.

281. *Youngstown Sheet & Tube Co. v. Sawyer*, 343 U.S. 579, 588 (1952).

282. See Olson & Woll, *supra* note 241, at 8 ("Although some directives are proper exercises of executive power, others are clearly usurpations of legislative authority.").

283. It is highly improbable that President Bush and his advisors were unaware of the potential conflict between his Stem Cell Decision and the NIHRA.

284. *Marbury v. Madison*, 5 U.S. (1 Cranch) 137, 163 (1803).

285. See Branum, *supra* note 7, at 59-60, 78-79 (emphasizing how few presidential directives have been modified, revoked or struck down).

Presidential acts.²⁸⁶ Thus, the Government might try to defend President Bush's Directive by arguing that similar directives issued by President Clinton went unchallenged and that President Bush's Directive "operates" in an area that has already been influenced by the actions of President Clinton and should be left to work its effect without court interference.²⁸⁷

Indeed, President Clinton's use of presidential directives to impose his policies on executive agencies²⁸⁸—like in the cases of his Embryo Decision and Cloning Decision mentioned earlier²⁸⁹—sometimes amounted to presidential lawmaking.²⁹⁰ And indeed, it appears that President Clinton's Embryo Decision,²⁹¹ which was never challenged although it too prohibited funding for certain kinds of embryo research in abrogation of NIHRA § 101, is almost identical in its legal circumstances to President Bush's Directive.²⁹² However, President Clinton's earlier illegal directives cannot immunize or cure the similar illegality of President Bush's Directive. The contention that one defective presidential action may draw legitimacy from

286. See *Youngstown*, 343 U.S. at 646 ("The Solicitor General lastly grounds support of the seizure upon nebulous, inherent powers never expressly granted but said to have accrued to the office from the customs and claims of preceding administrations.").

287. Branum alludes to this argument contending that President Bush was forced to give his Directive because of the Clinton Administration's allegedly illegal prying into this area, which required President Bush "to negate actions of President Clinton that had effectively taken the policy decision away from the legislature and placed it in the realm of the executive." See Branum, *supra* note 7, at 45.

288. See *Executive Orders and Presidential Directives: Hearing Before the House Subcomm. on Commercial and Administrative Law of the Comm. on the Judiciary*, 107th Cong. 2 (2001) [hereinafter *Hearing on Presidential Directives*] (criticizing this "attitude" and quoting President Clinton's Senior Domestic Policy Advisor, Paul Begalla, who said "Stroke of a pen, law of the land, kind of cool."); Gaziano, *supra* note 134, at 272-73; Kagan, *supra* note 170, at 2249, 2290; Strauss, *Presidential Rulemaking*, *supra* note 195, at 967.

289. See *supra* note 60.

290. See Branum, *supra* note 7, at 36-37 ("Clinton may have misused executive orders more blatantly than his predecessors . . ."); Kagan, *supra* note 170, at 2320-21 (contrasting President Clinton's invocation of "executive authority" with Justice Black's opinion in *Youngstown*); see also *Hearing on Presidential Directives*, *supra* note 288, at 2 (discussing the threat posed to legislative authority from the Executive branch's prevalent use of executive orders and citing President Clinton's administration as an example).

291. See *supra* note 60.

292. Neither directive mentions its source of authority nor was published in the Federal Register. See *supra* note 144. Also, both directives have an undefined form, and both run in clear violation of the NIHRA. President Clinton's Embryo Decision even blatantly disregarded the recommendations of a duly appointed EAB, the Human Embryo Research Panel. See *supra* Part I.B, notes 51-60 and accompanying text. It is worth noting that President Clinton's Cloning Decision also violates the NIHRA in much the same way as President Clinton's Embryo Decision and President Bush's Directive. See *supra* note 60. Yet, unlike President Bush's Directive that has been subject to ongoing challenges by Congress (see *supra* notes 121-31 and accompanying text), President Clinton's Embryo Decision was ratified by Congress's subsequent passing of the Dickey Amendment. See *supra* notes 63-68 and accompanying text. Interestingly, it appears that should Congress henceforth refrain from reenacting the Dickey Amendment as it has been doing every year, President Clinton's Embryo Decision would lose its "blanket of legitimacy" making it as illegal as President Bush's Directive.

the defectiveness of an earlier similar presidential action seems too feeble to hold water in court. Hence, although the aforementioned directives issued by President Clinton also appear to constitute a usurpation of legislative authority, they do not in any way justify such usurpation by President Bush's Directive. Rather, they too are challengeable as presidential lawmaking.

*B. Challenging the NIH's Withholding of Funding
for Research Involving hESCs*

Probably the most significant challenge to the NIH's actions pursuant to President Bush's Directive would rely on the fact that these actions were taken in spite of, and contrary to, the instructions of the NIHRA. As explained above, the NIHRA prevents NIH officers from withholding funding for scientific research due to ethical reasons.²⁹³ Hence, a challenge to the NIH's withholding of funding for research involving hESCs would contend that taking these actions without relying on the recommendation of a duly-established EAB constituted an imposition of a moratorium on research involving hESCs and an ongoing violation of the NIHRA.²⁹⁴

In other words, a challenge to the NIH's denial of funds for research involving hESC lines that do not comply with President Bush's Stem Cell Decision would argue that unless and until the NIH abides by the requirements of the NIHRA, it may not withhold funding from research involving any kind of hESCs and must allocate funding for such research projects subject only to their scientific merit.²⁹⁵ It therefore follows that the NIH is currently acting outside of its statutory authority and in violation of statutory limitations imposed on it,²⁹⁶ and thus its withholding of funding is unlawful and courts should set it aside.

*C. Challenging the NIH's Unilateral Repeal
of the Final Guidelines*

As explained above, the Repeal violated the APA's notice and comment requirements.²⁹⁷ A possible challenge posed to the Repeal would argue that it should have complied with the notice and comment requirements of 5 U.S.C. § 553, namely, that it should have taken place after giving interested parties an opportunity to comment on the planned withdrawal, weighing of the objections, and only then making an informed and properly reasoned decision on the withdrawal of the Final Guidelines. This kind of

293. See *supra* Part II.C, notes 251-52 and accompanying text.

294. 42 U.S.C. § 289a-1(b)(1), (3)-(5) (2000).

295. *Id.*

296. 5 U.S.C. § 706(2)(C) (2000).

297. See *supra* Part II.C, notes 254-71 and accompanying text.

challenge would stress that the NIH's failure to take these measures constituted a substantive flaw in the Repeal that conflicts with the APA's requirements.²⁹⁸ As a result, courts should set aside the Repeal, thereby reinstating the part of the Final Guidelines that regulates the funding of research involving hESCs. The practical implication of such a ruling would be that parties seeking federal funding for research involving hESC lines that do not comply with President Bush's Stem Cell Decision, would be able to do so subject to the more lenient standards of the reinstated Final Guidelines.²⁹⁹

*D. Challenging the NIH's Decision to Abide
by President Bush's Stem Cell Decision*

One may pose several challenges to the NIH's adoption and implementation of President Bush's Stem Cell Decision. First, one can argue that Acting Director Kirchstein's surrender of statutory authority to President Bush to make policy decisions for the NIH by adopting his Stem Cell Decision without actually using her own discretion was an abuse of her discretion to set policies for the NIH,³⁰⁰ which amounted to an unlawful abuse of discretion under the APA.³⁰¹ One could further contend that the Acting Director's adoption of President Bush's Stem Cell Decision as the NIH's own policy in its entirety—without any qualms or reservations, without paying respect to its underlying rationale and considering its alternatives,³⁰² without considering whether it promotes good public policy, and without weighing such considerations—may also tag her actions, and thus the actions of the NIH, as arbitrary and capricious.³⁰³

Furthermore, Moderate Unitarians would probably add that the Acting Director's omission of her own discretion in this matter was not in accordance with *her* statutory duty³⁰⁴ to make such a discretionary decision by herself under the authority granted to her in the Public Health Service Act.³⁰⁵ Should a court accept this argument, it may serve to justify an

298. 5 U.S.C. § 706(2)(D).

299. See *supra* Part I.C, notes 84-86 and accompanying text.

300. 42 U.S.C. § 282(b).

301. 5 U.S.C. § 706(2)(A).

302. It may be argued that the NIH's policy, which is in fact President Bush's Stem Cell Decision, did not properly weigh different aspects of the issues related to research involving hESCs. One could argue, for example, that the NIH's policy gives excessive weight to ethical and religious considerations while giving very little if any weight to important scientific and public policy considerations. See, e.g., Ryan Fujikawa, Note, *Federal Funding of Human Embryonic Stem Cell Research: An Institutional Examination*, 78 S. CAL. L. REV. 1075 (2005).

303. 5 U.S.C. § 706(2)(A); see also *supra* Part II.C.

304. *Id.* § 706(2)(C).

305. 42 U.S.C. § 282(b). This argument would be based on the Moderate Unitarian reading of statutory duties as applying exclusively to the specific executive officers named

injunction against the NIH, enjoining it from enforcing President Bush's Directive and instructing the Director of the NIH to use her own discretion in making a decision regarding the NIH's funding policy of research involving hESCs (to the extent the NIHRA leaves this issue to the discretion of the Director of the NIH).

It is worth adding a few words in this context on the standard of review courts would probably apply to such challenges. Courts generally grant agencies' discretionary decisions and actions a great measure of deference and are not easily persuaded to set them aside.³⁰⁶ However, in order to merit this measure of deference, agency decisions must be based on the agency's expertise in the area of regulation it is charged with implementing.³⁰⁷ Without demonstration of reliance on such expertise by the agency, courts would not defer to the agency's decision.³⁰⁸ Accordingly, since the NIH's policy on the funding of research involving hESCs does not reflect its expertise on this issue, but merely its reliance on the President's opinions,³⁰⁹ courts would probably not grant it the deference they normally would have under the *Chevron* Doctrine.³¹⁰ Furthermore, courts only defer to and uphold agency decisions that are properly reasoned.³¹¹ According to the Supreme Court, this is especially true where,

in the authorizing statute. However, it is important to note that to date there is no court decision accepting such Moderate Unitarian contentions, so it is hard to assess how willing courts would be to entertain this argument.

306. See *Chevron U.S.A. Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 842-44 (1984) ("We have long recognized that considerable weight should be accorded to an executive department's construction of a statutory scheme. . . .").

307. See *Pub. Citizen Health Research Group v. Tyson*, 796 F.2d 1479, 1505 (D.C. Cir. 1986) ("While we acknowledge our deference to the agency's expertise in most cases, we cannot defer when the agency simply has not exercised its expertise.").

308. *Id.*

309. Despite his outspoken efforts to inform himself prior to making his Stem Cell Decision, President Bush may not be considered an expert in the area of research involving hESCs.

310. In addition, in the NIHRA, Congress directly spoke on the precise question of withholding of federal funding for scientific research on ethical grounds and its instruction on this matter constitutes an explicit congressional prohibition on actions such as those taken by the NIH with respect to the funding of research involving hESC. Therefore, courts should not grant *Chevron* deference to the NIH's policy on funding for research involving hESCs. See *Chevron*, 467 U.S. at 842-43. It is also worth mentioning that, according to Stack, courts should only grant *Chevron* deference to agency actions and decisions that follow presidential directives where a statute expressly grants authority to make such a decision specifically to the President. See Stack, *supra* note 175, at 263, 268-69, 307, 310-11.

311. See *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) ("[T]he agency must examine the relevant data and articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'") (citation omitted); see also *BellSouth Corp. v. FCC*, 162 F.3d 1215, 1222 (D.C. Cir. 1999) ("Where the agency has failed to provide a reasoned explanation, or where the record belies the agency's conclusion, we must undo its action." (quoting *Petroleum Communications, Inc. v. FCC*, 22 F.3d 1164, 1172 (D.C. Cir.1994))).

as here, the agency is repealing a previous policy.³¹² The NIH failed to provide a reasoned explanation for its actions and only justified the Repeal and its adoption of President Bush's Stem Cell Decision as its policy by stating that these measures were compatible with President Bush's Stem Cell Decision.³¹³ Arguably, even under the assumption that agency action may be greatly influenced by presidential policy preferences, this hardly seems like the kind of reasoning that courts would accept in order to uphold an agency's decision. Hence, it is likely that in a challenge to the NIH's policy—like the ones mentioned above—a court would not grant it *Chevron* deference, but would find the policy lacking in reasoning and would thus set it aside as arbitrary and capricious.

In conclusion, an interesting question arises: if there are so many ways and reasons to challenge President Bush's Directive and its implementation by the NIH, how can we explain the fact that no one has ever raised such challenges in court? One plausible explanation may lie in Dean Kagan's description of a shift in what Strauss called the "psychology of government"³¹⁴—namely, that executive officers have become so "desensitized" to the accelerating use of presidential directives that impose policies on them and have become so used to the Constitutional Unitarian rhetoric accompanying such directives that they no longer doubt the applicability or validity of such directives. A second parallel phenomenon apparently has accompanied this phenomenon and intensified its effects. The media, and as a result the general public, have grown "numb" to the ever increasing intrusions of presidential directives—especially during the Clinton and Bush Administrations³¹⁵—into what used to be perceived as the sole domain of executive agencies' discretion.³¹⁶ By the time President Bush gave his Directive, the public, the media, and the agencies themselves had grown so accustomed to such presidential assertions of authority that evidently no one proceeded to challenge what seemed to be yet another assertion of the rising presidential power, no more or less outrageous than many others before it. Add to these factors what Gaziano describes as a low level of public understanding of the legal foundation and proper uses

312. See *State Farm*, 463 U.S. at 41-42 ("[A]n agency changing its course by rescinding a rule is obligated to supply a reasoned analysis for the change beyond that which may be required when an agency does not act in the first instance.").

313. See *supra* text accompanying note 120.

314. Kagan, *supra* note 170, at 2299; Strauss, *Presidential Rulemaking*, *supra* note 195, at 986.

315. See generally Strauss, *Presidential Rulemaking*, *supra* note 195; Branum, *supra* note 7; Olson & Woll, *supra* note 241 (discussing President Clinton's presidential directives).

316. For a similar argument related to the regulation of funding of research involving hESCs, see Branum, *supra* note 7, at 46-47.

of presidential directives³¹⁷ and the legal community's preoccupation with the debate over the "unitary executive,"³¹⁸ and the result is that President Bush's Directive and its progeny were allowed to pass unchallenged.

Another, less dramatic explanation as to why President Bush's Directive and the ensuing NIH policy remain uncontested may be that no party partaking in research involving hESCs in the United States has been ready and willing to spend the time, money, and effort necessary to challenge them in court. Despite these hurdles, I hope that this Article would serve to encourage interested parties to challenge President Bush's Directive and its implementation by the NIH.

CONCLUSION

For over six and a half years, President Bush's Stem Cell Decision has been dictating the nature and extent of scientific research involving human embryonic stem cells. Yet, astonishingly, despite being the subject of a boisterous debate, its legality, as well as that of the actions taken by the NIH to carry it out, have never been questioned nor ascertained. This Article sought to fill this vacuum.

This Article has shown that even under the most permissive assumptions President Bush's Directive cannot be reconciled with NIHRA § 101. This Article further demonstrated that the actions taken by the NIH to implement President Bush's Directive constituted clear violations of the NIHRA and the APA—the extent of which depends on one's viewpoint in the "unitary executive" debate. Finally, this Article argued that these flaws render both President Bush's Directive and the ensuing actions taken by the NIH illegal and thus challengeable in court. I anticipate that such challenges would result in striking down President Bush's Directive and in setting aside the NIH's adoption of his Stem Cell Decision as its policy. Furthermore, such a challenge may also prompt a court to overrule the NIH's withdrawal of the Final Guidelines' language dealing with research involving hESCs and to reinstate language allowing federal funding for types of research involving hESCs disallowed by President Bush's Directive.

An interesting issue that remains, which may justify a separate, more elaborate inquiry, is what President Bush and the NIH could do in order to *legally* enforce President Bush's Stem Cell Decision. Arguably, the NIH may entrust the entire issue of the ethical soundness of research involving hESCs to an Ethics Advisory Board, which it could establish pursuant to the NIHRA. Alternatively or additionally, President Bush might use his

317. Gaziano, *supra* note 134, at 269-70.

318. *See supra* Part II.B.3.a.i.

authority to direct executive agencies in a less controversial manner to pile up procedural requirements or obstacles for any attempt to actually fund such research involving hESCs, so as to render such funding practically impossible or prohibitively burdensome.

Though it is hard to anticipate whether the current Administration would elect to take any of these measures or whether President Bush's Directive and the NIH's ensuing actions will eventually face a challenge in court, it is prudent to assume that President Bush's Stem Cell Decision will eventually be discarded. With the newly formed Democratic majority in Congress, we should probably expect more bills akin to the Stem Cell Research Act of 2005, which would seek to impose federal funding for research involving hESCs, though potential presidential vetoes await. Furthermore, rapid encroachments on the efficacy of the current federal government's policy by state funding and international research, increasing public pressure to fund research involving hESCs, development of new techniques to produce hESCs without destroying embryos, and the United States' incentive to stay in the forefront of scientific research will all, sooner or later, bring the demise of the current policy in favor of one that is more permissive. President Bush's Stem Cell Decision swims against the current and—as other cases of ethically controversial though useful scientific technologies teach us—will eventually yield to progress; it is only a matter of time. Yet, the way this chapter in our regulatory history will end may have bearing on crucial issues regarding the nature of the Chief Executive and the extent of its “unitariness.” Will it finally be limited by courts or by Congress, or will it remain uninhibited as is reflected in President Bush's Directive? In addition, hopefully Congress will take heed of the regulatory knot described in this Article as a cue that the time has finally come to create a federal mechanism for the formulation of government-wide bioethical policies, as other countries have done.

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THE REGULATION OF GENETIC ASPECTS OF DONATED REPRODUCTIVE TISSUE—THE NEED FOR FEDERAL REGULATION

Yaniv Heled¹

It is estimated that egg and sperm donations account for more than 60,000 births every year in the United States. However, surprisingly, and despite common misconceptions, there are no federal requirements and barely any state requirements to screen and test sperm and egg donors for genetic diseases. The only nationwide standards for genetic screening and testing of donated reproductive tissue are guidelines created by professional organizations, but compliance with those guidelines is voluntary so they cannot be enforced effectively. Furthermore, the few reported cases involving children born from genetically-compromised reproductive tissue illustrate the court system's failure to afford such children and their families the relief they need and deserve. With a continuing rise in the number of babies born each year who are conceived with donated reproductive tissue, it is necessary to create a regulatory framework requiring the screening and testing of reproductive tissue donors for genetic diseases. This article makes the case for federal regulation of the genetic aspects of donated reproductive tissue under the authority granted to the FDA by the Public Health Service Act.

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I. INTRODUCTION

Imagine John and Jane, a couple with a common problem experienced by one in every six couples in the United States:² infertility.³ John and Jane seek medical advice and discover that one of them is sterile. They decide to take advantage of one of the numerous assisted reproductive technologies (ART)⁴ now available to couples suffering from difficulties such as theirs and start looking for a suitable donor. Browsing through online donor catalogues, they find a donor whose sperm or eggs they would like to use. The sperm/egg bank assures them that their chosen donor—a young, tall, good-looking, gifted, intelligent, and athletic graduate student—has undergone careful screening and was tested⁵ for health problems as required by all applicable federal and state laws. Having received such assurances, John and Jane attempt to conceive using the donated reproductive tissue (DRT)⁶ they have procured from the bank. They are successful and soon thereafter Jane gives birth to twins, Jean and Juan. Alas, after the birth, Jean is

² See S. Rep. No. 102-452, at 1 (1992); ISLAT Working Group, *ART into Science: Regulation of Fertility Techniques*, 281 Science 651, 651 (1998) [hereinafter ISLAT Working Group].

³ Infertility is commonly defined as the inability to get pregnant after trying for one year. See Centers for Disease Control and Prevention (CDC), Assisted Reproductive Technology: Home, <http://www.cdc.gov/art> (last visited May 9, 2010).

⁴ According to the CDC, ART consists of all clinical treatments and laboratory procedures—including the handling of human oocytes and sperm, or embryos—conducted with the intent of conceiving, e.g., in-vitro fertilization, gamete intrafallopian transfer, zygote intrafallopian transfer, sperm, oocyte or embryo donation, and gestational surrogacy. See Implementation of the Fertility Clinic Success Rate and Certification Act of 1992—A Model Program for the Certification of Embryo Laboratories, 64 Fed. Reg. 39374, 39383 (CDC July 21, 1999) [hereinafter CDC Model Program].

⁵ For purposes of this article, “testing” is defined as any procedure involving direct clinical examination of a potential donor or her tissue, whereas “screening” is any inference of clinical information through indirect examination of a donor’s background. For example, questioning a potential donor in order to identify possible genetic risk factors in her family’s medical history is a screening procedure, while verifying that her genes do not contain certain genetic mutations by attempting to identify certain genetic markers in a cell sample taken from her would be considered testing. Notably, direct testing of the genes of a potential donor is not the only readily available method of testing donor candidates. For example, ECG could assist in identifying heart conditions whose genetic background may be unclear or otherwise difficult to ascertain. See Barry J. Maron et al., *Implications of Hypertrophic Cardiomyopathy Transmitted by Sperm Donation*, 302 JAMA 1681, 1684 (2009) (reporting that an electrocardiogram could assist in identifying 80-95% of the cases of hypertrophic cardiomyopathy in adults with left ventricular hypertrophy, a hereditary and potentially lethal cardiac anomaly).

⁶ The term “donated reproductive tissue” includes all forms of reproductive cells that can be used in ART, namely sperm and ova (eggs) in different developmental stages and in different media.

diagnosed with cystic fibrosis (CF)⁷ and a few years later Juan is diagnosed as suffering from autosomal dominant polycystic kidney disease (ADPKD).⁸ John and Jane are devastated. Inquiries conducted by their (very expensive) attorneys reveal that their donor was a carrier of a CF mutation. Moreover, after overcoming numerous legal hurdles, John and Jane find out that their donor's aunt and grandmother died from kidney failure. They sue the DRT bank for regular and punitive damages under numerous causes of action including negligence, products liability, wrongful life, infliction of emotional distress and fraud. Yet, the court rejects the majority of their claims as a matter of law. Furthermore, the court is unsympathetic to the family's situation and holds that children do not have the "right to be born free of diseases" regardless of whether they were conceived naturally or through ART. The tissue bank issues a press release truthfully stating that it is meticulously following and is in full compliance with all federal and state legislation and regulation. It quickly reaches a quiet and relatively cheap settlement with the Does regarding their remaining claims; if it is a member of a professional accreditation organization, such as the American Association of Tissue Banks (AATB), it might lose its membership for a short while.

This hypothetical scenario illustrates actual cases litigated in the United States⁹ and foreshadows more that are likely to be brought under the current federal and state

⁷ CF is a hereditary disease whose symptoms usually appear shortly after birth and include digestion problems, breathing difficulties and respiratory infections; in the past it was almost always fatal in childhood, but nowadays patients commonly live long past childhood. CF is an autosomal recessive condition, meaning that in order to have an affected child both parents must carry the mutated gene and pass it along to the child, which has a one in four (1:4) likelihood of happening with each pregnancy. See National Human Genome Research Institute, Glossary, <http://science.education.nih.gov/supplements/nih1/genetic/other/glossary/act1-gloss2.htm> (last visited May 9, 2010); National Genome Research Institute, Learning about Cystic Fibrosis, <http://www.genome.gov/10001213> (last visited May 9, 2010).

⁸ According to the Human Genome Research Institute, ADPKD is one of the most common forms of polycystic kidney disease (PKD), a genetic disorder characterized by the growth of numerous cysts in both kidneys. As the disease progresses, the cysts get filled with fluid and slowly replace much of the normal mass of the kidneys, thus reducing kidney function and leading to kidney failure. PKD can also cause cysts in the liver and problems in other organs such as the pancreas, the heart and the brain, as well as high blood pressure (hypertension), abdominal wall hernias, and more. As indicated by its name, ADPKD is an autosomal dominant disease, which means that if a child inherits one copy the ADPKD gene he or she will likely develop the disease. Each child of a parent having an ADPKD gene has a 50-50 chance of inheriting the ADPKD gene. See National Human Genome Research Institute, Learning About Autosomal Dominant Polycystic Kidney Disease, <http://www.genome.gov/20019622> (last visited May 9, 2010).

⁹ See *Johnson v. Superior Court (Johnson II)*, 124 Cal. Rptr. 2d 650, 666 (Cal. Ct. App. 2002) (holding that the kidney disease of a child born from DRT (DRT child) was caused by a gene in the sperm rather than by either the sperm bank or the bank's physician's actions in improperly approving the sperm donor, and thus, that the child could not recover general damages or lost earnings); *Becker v. Schwartz*, 386 N.E.2d 807, 811-12 (N.Y. 1978) (rejecting "wrongful life" as a cognizable cause of action and holding that a child does not have a fundamental right to be born

regulation of DRT. Yet, an even greater source of concern is the vast and growing number of children born every year in the United States from DRT¹⁰ who, to their and their families' misfortune, might become a part of such a tragedy.¹¹ According to the Centers for Disease Control and Prevention (CDC), in 2006 there were 5,393 babies born in the United States from donated eggs and embryos.¹² There is no current data regarding the number of babies born from donated sperm,¹³ but a survey conducted by the former Office of Technology Assessment (OTA) estimated the number of births from artificial insemination (AI) by a donor at 30,000 per year in 1986-87.¹⁴ In 1998, the ISLAT

as a whole, functional human being); *Paretta v. Medical Officers for Human Reproduction*, 760 N.Y.S.2d 639, 644 (N.Y. Sup. Ct. 2003) (re-stating that a child does not have the right to be born free of genetic defects, regardless of how she was conceived, and thus, that a DRT child born with CF did not suffer a legally cognizable injury and her parents did not have a valid claim for damages for the emotional distress they experienced as a result of having a child with a genetic disease).

¹⁰ See Elizabeth A. Conrad et al., *Current Practices of Commercial Cryobanks in Screening Prospective Donors for Genetic Disease and Reproductive Risk*, 41 Int. J. Fertil. 298, 303 (1996); see also CDC, *Assisted Reproductive Technology Success Rates—National Summary and Fertility Clinics Reports 2004*, 52 (2006) [hereinafter CDC 2004 Report]; Peggy Orenstein, *Your Gamete, Myself*, N.Y. Times Magazine, July 15, 2007, at 36.

¹¹ There are no official statistics regarding the transmission of genetic diseases through DRT. See Conrad, *supra* note 10, at 299. Thus, it is difficult to accurately evaluate the risks of genetic diseases involved in using DRT.

¹² See CDC, *2006 Assisted Reproductive Technology Success Rates: National Summary and Fertility Clinic Reports* 59 (2008). Unofficial estimates currently speak of 7,000-10,000 births from egg donation a year.

¹³ The author is not aware of any source of statistical data regarding the number of donor sperm specimens sold or of babies born from such DRT yearly in the United States. The legislation authorizing CDC to collect information from "embryo laboratories" regarding egg donations and IVF success rates does not apply to sperm donations and sperm use success rates. See *infra* notes 32-33. Thus, there are no official statistics regarding the number of semen specimens sold and children resulting from artificial insemination (AI) in the United States each year.

¹⁴ See Office of Technology Assessment (OTA), *Artificial Insemination Practice in the United States: Summary of a 1987 Survey* 3 (Aug. 1988) [hereinafter *OTA 1988 Survey*]. According to the survey, in 1986-87, 172,000 women underwent artificial insemination, resulting in about 65,000 births, 35,000 of which were from artificial insemination by the husband. See *id.*

With respect to DRT, one should distinguish between "directed donations," in which the recipient receives DRT from a person whom she knows and is known by prior and unrelated to seeking the donation, and anonymous donations, in which the recipient does not know the identity of the donor (or—in case the donor agrees to expose his/her identity—the recipient knows who the donor is but did not know him or her prior to the acquisition of the DRT). It is important to note that the discussion of DRT in this article focuses almost exclusively on anonymous donations.

Working Group estimated that egg and sperm donations account for more than 60,000 births every year.¹⁵ Yet, despite the significance of these numbers, there is a dearth of state law¹⁶ and a total lack of federal law regulating the genetic aspects of DRT.¹⁷ Court decisions addressing the failure of DRT institutions¹⁸ to screen and test donors for genetic

¹⁵ See ISLAT Working Group, *supra* note 2, at 652. Due to a lack of accurate data, it is difficult to determine whether these numbers have grown or dropped as a result of advancements in ART. Regardless, it is clear that the number of DRT children is very significant. See Judith F. Daar & Robert G. Brzyski, *Genetic Screening of Sperm and Oocyte Donors: Ethical and Policy Implications*, 301 JAMA 1702, 1702 (2009) (reporting that nearly 3 in every 100 births in the United States is attributable to some form of assisted conception and arguing that the numbers of births using DRT have been steadily increasing since the introduction of IVF in 1978).

¹⁶ Only two states—New York, and Ohio—require genetic screening and testing of DRT donors for some genetic diseases. See *infra* Part II.B.

¹⁷ See Maron et al., *supra* note 5, at 1681, 1683 (describing a series of cases in which a genetically inherited disease was transmitted through anonymous sperm donation and characterizing this type of risk as “a problem largely unappreciated by the medical community and agencies regulating tissue donation”; “[a]lthough not required by FDA, some sperm banks test for cystic fibrosis, thalassemia anemia, sickle cell trait, Tay-Sachs, and other genetic diseases . . .”) (emphases added).

In this article, the term “genetic aspects of DRT” includes (1) screening and testing of DRT donors based on genetic criteria, (2) keeping genetic information on record, (3) informing DRT recipients about relevant donor genetic information and its potential ramifications, and (4) notification of proper authorities and institutions engaging in collection and distribution of DRT and recipients of adverse events having a genetic background or suspected as having a genetic background. For purposes of this article, this term does not apply to genetic aspects of any infectious diseases, e.g., viral infection (such as HIV, herpes, etc.) that influences the nucleic acid makeup of human cells.

The term “genetic aspects of DRT” also does not include the genetic screening and testing of potential DRT recipients. Arguably, genetic screening and testing of DRT recipients would be less cost-effective and more cumbersome than the screening and testing of potential DRT donors. This is because DRT donors (mostly sperm donors) are normally the source of a large number of DRT specimens used to conceive many DRT children while any DRT recipient would normally have a few children at most. Admittedly, only a minority of the candidates eventually become DRT donors, yet DRT programs may test only potential donors that make it through earlier selection stages. Also, a requirement for genetic screening and testing of potential DRT donors rather than DRT recipients is more feasible and more defensible from a privacy perspective because DRT donors normally submit themselves to medical evaluations as part of the selection process and thus, are more readily available and likely to give their consent to have their genetics tested.

¹⁸ For purposes of this article, a DRT institution is any individual or entity engaged in the manufacture of DRT; “manufacture,” according to the FDA, includes but is not limited to “any or all steps in the recovery, processing, storage, labeling, packaging, or distribution of any human cell or tissue, and the screening or testing of the cell or tissue donor.” See 21 C.F.R. § 1271.3(e) (2005). DRT institutions include, e.g., sperm banks and institutions that harvest donor oocytes as

diseases are sparse and ambivalent. Thus, the only means of protection from genetic disease afforded to DRT children and their families are the standards set by professional organizations.¹⁹ However, membership in such organizations is purely voluntary and non-compliance does not seem to carry any real sanctions.²⁰ Hence, currently, in the United States, there is no effective protection of DRT recipients from acquiring genetically defective DRT or of DRT children from having such diseases even where there *are* effective means of testing for and preventing the transmission of such diseases.

Despite repeated warnings since the late 1970s regarding the insufficiency of genetic screening and testing of DRT and subsequent calls for regulation,²¹ there are no signs that the current framework of regulation of genetic aspects of DRT (or lack thereof) is about to change. Legislators, in general, are averse to legislating about issues pertaining to human reproduction²² and regulators show a similar disinclination.²³ It thus appears that no one is going to address this void unless forced to do so by the occurrence of a highly publicized tragedy. Furthermore, additional discoveries of genetic bases of diseases and development of means of testing for such diseases in the future would only accentuate the problems existing under the current regulatory scheme. Fortunately, there is a way to correct the situation and fill the regulatory vacuum before more tragedies occur.

On May 25, 2005 the FDA promulgated regulations pertaining to communicable disease aspects of DRT, including requiring the screening and testing of DRT donors for infectious diseases.²⁴ Yet, the FDA refrained from taking similar steps with respect to the genetic aspects of DRT.²⁵ I argue that by stepping into the area of regulation of DRT, the

well as small clinics that serve smaller populations so long as they manufacture donor DRT. This definition of DRT, however, does not include clinics that merely harvest DRT for directed donations.

¹⁹ See *infra* Part IV (discussing professional standards set by the American Society for Reproductive Medicine (ASRM) and the American Association of Tissue Banks (AATB)).

²⁰ See *infra* notes 181 and 196 and accompanying text.

²¹ See *infra* Part II.D.1.

²² See George J. Annas, *The Shadowlands—Secrets, Lies, and Assisted Reproduction*, 339 *New Eng. J. Med.* 935, 937 (1998); Stacy Huse, *The Need for Regulation in the Fertility Industry*, 35 *U. Louisville J. Fam. L.* 555, 556 (1996-1997).

²³ See Cynthia B. Cohen, *Unmanaged Care: The Need to Regulate New Reproductive Technologies in the United States*, 11 *Bioethics* 348, 357 (1997); Richard A. Merrill, *Human Tissues and Reproductive Cloning: New Technologies Challenge FDA*, 3 *Hous. J. Health L. & Pol'y* 1, 63 n.332 (2002).

²⁴ FDA, Guidance for Industry, Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products, 69 F.R. 29786-01 (May 25, 2004) [hereinafter *FDA Final Donor Eligibility Rule*].

²⁵ The FDA provided no explanation for its avoidance of the area of genetic aspects of DRT. See *infra* Part IV (discussing possible reasons for the FDA's inaction).

FDA has created the necessary infrastructure for expanding its regulatory scheme to include the regulation of the genetic aspects of DRT and has positioned itself as the preferable regulator of this area. The FDA's authority under the Public Health Service Act (PHSA)²⁶ provides it with ample authority to regulate not only the communicable diseases aspects of DRT but also their genetic aspects, as is done in other countries. This article makes the case for such federal regulation of the genetic aspects of DRT by the FDA.

Part II of this Article will describe the current regulation of DRT in the United States with emphasis on its genetic aspects and the compelling public policy reasons for the regulation of this area. Part III will survey the regulation of genetic screening and testing of DRT in the European Union, the United Kingdom and Ireland and highlight some of the mechanisms they employ to overcome reoccurring problems typical to such regulation. Implementing some of the mechanisms applied abroad to the unique circumstances of the United States, Part IV will offer a framework for the regulation of genetic aspects of DRT by the FDA and will discuss some of the issues involved in and obstacles to such regulation. Part V will conclude this Article with a call for the FDA to rise to the challenge of filling the regulatory vacuum.

II. THE REGULATION OF GENETIC SCREENING AND TESTING OF DONATED REPRODUCTIVE TISSUE IN THE UNITED STATES

The regulation of DRT in the United States has been repeatedly described as lacking in its protection of DRT recipients and DRT children.²⁷ This Part will explain why this criticism is particularly justified with respect to the regulation of the genetic aspects of DRT.

A. Federal Regulation

Although the federal government has regulated several aspects of ART,²⁸ there is no federal law addressing the genetic aspects of DRT. The lack of such regulation is peculiar in light of the federal government's actual involvement in the regulation of two aspects of DRT, specifically the creation of a model program for the accreditation of fertility clinics to be carried out by the states²⁹ and the regulation of DRT as human

²⁶ Public Health Service Act (PHSA), Ch. 373, 58 Stat. 682 (July 1, 1944), *codified at* 42 U.S.C. §§ 201–300, Ch. 6A.

²⁷ See generally OTA, *Infertility: Medical and Social Choices* 24–26 (1988) [hereinafter *OTA's Infertility Report*]; Huse, *supra* note 22, at 571–72; Charles Marwick, *Artificial Insemination Faces Regulation, Testing of Donor Semen, Other Measures*, 260 JAMA 1339 (1988); Judith Lynn Bick Rice, *The Need for Statutes Regulating Artificial Insemination by Donors*, 46 Ohio St. L.J. 1055 (1985).

²⁸ See *infra* Parts II.A.1–II.A.2.

²⁹ See CDC Model Program, *supra* note 4, at 39374.

tissue.³⁰ Both regulatory schemes stop just short of addressing the genetic aspects of DRT.

1. The Regulation of ART by the CDC

In 1992, concerned with information indicating that some fertility clinics misled patients by making false and exaggerated representations of success rates in achieving pregnancies and provided substandard services,³¹ Congress legislated the Fertility Clinic Success Rate and Certification Act of 1992 (FCSRCA).³² FCSRCA instructed the CDC to develop a model program for the accreditation of embryo laboratories³³ which would be carried out by the states.³⁴ The CDC published the Model Program devised under FCSRCA in the Federal Register on July 21, 1999.³⁵ Although FCSRCA strove to regulate the quality of embryo laboratories, it did not include any requirement for the assurance of the safety of the procedures employed by such laboratories, and so neither did the resulting CDC Model Program.³⁶ Thus, although Congress may have sought to protect consumers acquiring the services of fertility clinics from false representations and poor quality of services,³⁷ it neglected to create a more comprehensive regulatory scheme that would protect DRT recipients and DRT children from such hazardous practices as improper testing of DRT for genetic diseases.

³⁰ 21 C.F.R. § 1271 (2009) [hereinafter Human Tissue Regulations].

³¹ See S. Rep. No. 102-452, at 2565-67 (1992); 137 Cong. Rec. E4145-02 (1991) (statement of Rep. Wyden).

³² 42 U.S.C. § 263a-1 (1992).

³³ FCSRCA § 8 defines an “embryo laboratory” as “a facility in which human oocytes are subject to assisted reproductive technology treatment or procedures based on manipulation of oocytes or embryos which are subject to implantation.” 42 U.S.C. § 263a-7 (1992).

³⁴ 42 U.S.C. § 263a-2 (2008).

³⁵ See CDC Model Program, *supra* note 4, at 39374.

³⁶ 42 U.S.C. § 263a-2(d) (2008).

³⁷ See note 31 *supra*. Notably, Congress was well aware that FCSRCA was far from providing a sufficiently comprehensive protection for ART consumers in general, and in particular with respect to genetic aspects of DRT. Addressing the House of Representatives in his presentation of FCSRCA, Rep. Wyden said: “I would like to alert my colleagues to another area deserving of vigorous Congressional oversight—the \$170 million artificial insemination industry. A study by the Office of Technology Assessment has revealed a startling lack of oversight, particularly in doctor’s offices, which could have significant adverse public health effects. . . . [H]alf [of the physicians who provide AI services] don’t screen for genetic defects.” 137 Cong. Rec. E4145-02 (1991) (statement of Rep. Wyden).

Even further demonstrating its lack of effectiveness, the CDC Model Program is only voluntary for states³⁸ and embryo laboratories alike.³⁹ Thus, even had the CDC Model Program been sufficiently comprehensive, it would probably not have contributed to the safety of DRT children.

2. The FDA's Human Tissue Regulations

Repeated calls for a comprehensive scheme of federal regulation of donated tissue, including DRT,⁴⁰ prompted the FDA to announce in March 1997 that it intended to create a regulatory scheme for "cellular and tissue based products"⁴¹ (including DRT) which would include donor eligibility standards and donor screening and testing requirements.⁴² After a lengthy "notice and comment" process,⁴³ in January 2001 the FDA published the first of three installments of regulations that would eventually become

³⁸ 42 U.S.C. § 263a-2(e) (2008). Under the Anti-Commandeering Doctrine, the federal government may not instruct the states to adopt legislation but rather may merely try to convince them to do so through incentives. *See New York v. United States*, 505 U.S. 144, 166-69 (1992); *Printz v. United States*, 521 U.S. 898, 924-25 (1997). Hence FCSRCA could not compel the states to apply for the CDC Model Program. Notably, except for coverage of inspections of fertility institutions by funds collected from participating DRT institutions, the CDC Model Program does not seem to include any real incentive for the states to apply to participate in it. *See* FCSRCA § 7; CDC Model Program, *supra* note 4, at 39382. This lack of incentive may account, at least in part, for the fact that no state has submitted a request with the CDC to join the Model Program. Telephone Interview with CDC Division of Reproductive Health Helpdesk representative, Feb. 23, 2010 (on file with author).

³⁹ *See* CDC Model Program, *supra* note 4, at 39382.

⁴⁰ *See* FDA, *Reinventing the Regulation of Human Tissue* (Feb. 1997) [hereinafter *Reinventing the Regulation of Human Tissue*], available at <http://www.fda.gov/BiologicsBloodVaccines/TissueTissueProducts/RegulationofTissues/ucm136967.htm>.

⁴¹ *See generally* Proposed Approach to Regulation of Cellular and Tissue-Based Products: Availability and Public Meeting, 62 Fed. Reg. 9721 (FDA Mar. 4, 1997) [hereinafter *FDA's Proposed Approach*]. Notably, as early as 1993, the FDA published an interim rule that required the screening and testing of some human tissue for HIV and hepatitis. *See* Human Tissue Intended for Transplantation, 58 Fed. Reg. 65514 (FDA Dec. 14, 1993). However, this rule, whose final version was published in 1997, 62 Fed. Reg. 40429 (FDA July 29, 1997), did not apply to DRT. *See* 21 C.F.R. § 1270.3(j)(5) (2005).

⁴² *See Reinventing the Regulation of Human Tissue*, *supra* note 40, at 1 ("The agency would require infectious disease screening and testing be done for cells and tissues transplanted from one person to another.").

⁴³ *See* 66 Fed. Reg. 5448 (FDA Jan. 19, 2001) (describing the process); 69 Fed. Reg. 29786, 29786-87 (FDA May 25, 2004) (same).

the Human Tissue Regulations,⁴⁴ which required all DRT institutions to register with the FDA.⁴⁵ In May 2004, the FDA published its draft Donor Eligibility Rule,⁴⁶ which eventually went into effect on May 25, 2005.⁴⁷

Under the FDA's Final Donor Eligibility Rule, DRT banks must make donor eligibility determinations⁴⁸ based on donor screening and testing for an array of infectious diseases that might pass to children born through the use of DRT, including HIV-1 and HIV-2, human cytomegalovirus, hepatitis B and C, syphilis, gonorrhea, chlamydia, West Nile virus and more.⁴⁹ Such donor eligibility determinations must be based on an assessment of the donor's risk factors in light of his or her medical records⁵⁰ and the results of tests performed on the donated tissue,⁵¹ with additional specific requirements

⁴⁴ Human Cells, Tissues, and Cellular and Tissue-Based Products: Establishment of Registration and Listing, 66 Fed. Reg. 5447, 5448 (FDA Jan. 19, 2001).

⁴⁵ 21 C.F.R. § 1271.1 (2005). For inclusion of DRT institutions in the Human Tissue Regulations, see 21 C.F.R. § 1270.10(a)(4)(i)(c). According to the FDA's Human Cell and Tissue Establishment Registration (HCTERS), as of May 2009 there were 554 establishments involved in the recovery, processing and distribution of semen and 472 establishments involved in recovery, processing and distribution of oocytes registered with the FDA. See FDA, Find a Tissue Establishment, <http://www.fda.gov/cber/tissue/tissregdata.htm> (last visited May 9, 2010).

⁴⁶ See generally *FDA Final Donor Eligibility Rule*, *supra* note 24.

⁴⁷ *Id.* at 29786. The third "installation" of the Human Tissue Regulations was published in its final form in Nov. 2004 and became effective on May 25, 2005. See Current Good Tissue Practice for Human Cell, Tissue, and Cellular and Tissue-Based Product Establishments: Inspection and Enforcement, 69 Fed. Reg. 68612 (FDA Nov. 24, 2004).

⁴⁸ 21 C.F.R. § 1271.50 (2005).

⁴⁹ 21 C.F.R. §§ 1271.3(r), 1271.50, 1271.75, 1271.80, 1271.85 (2005). See also FDA, Testing HCT/P Donors: Specific Requirements, <http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm151757.htm> (last visited June 17, 2010). Tissue manufacturers are also under an obligation to screen and test donors for diseases not enumerated in the *FDA Final Donor Eligibility Rule* that (1) carry a risk of transmission, (2) potentially have sufficiently severe effects and (3) may be screened or tested for. See 21 C.F.R. § 1271.3(r)(2) (2005).

⁵⁰ 21 C.F.R. § 1271.75 (2005). Although the regulations do not mention specific "risk factors" that would render a person ineligible to donate tissue, such risk factors are enumerated in a "Guidance for Industry" document released by the FDA in February 2007. See Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products: Availability, 72 Fed. Reg. 9007 (FDA Feb. 28, 2007) [hereinafter *FDA's Guidance for Industry Announcement*].

⁵¹ 21 C.F.R. § 1271.85 (2005).

set forth for the testing of DRT.⁵² “A donor whose specimen tests reactive”⁵³ or who is “identified as having . . . [a] risk factor for or clinical evidence of any”⁵⁴ of the diseases enumerated in the Human Tissue Regulations is deemed ineligible to donate.⁵⁵ In addition, tissue manufacturers must investigate and report to the FDA any serious adverse reaction related to donated tissue.⁵⁶ Notably, the FDA’s Final Donor Eligibility Rule was complemented by a “Guidance for Industry,”⁵⁷ which reflected the “FDA’s current thinking” on eligibility determination by tissue manufacturers.⁵⁸

Despite its outspoken intention to create a comprehensive regulatory framework for cells and tissue-based products, which “would provide physicians and patients with the assurance of safety that the public has come to expect from . . . products overseen by the FDA,”⁵⁹ from the outset, the FDA narrowed the possible scope of its regulatory scheme and limited it to the prevention of infectious diseases.⁶⁰ Most importantly, in

⁵² DRT must also be tested for *Chlamydia trachomatis* and *Neisseria gonorrhea*. See 21 C.F.R. § 1271.85(c) (2005).

⁵³ 21 C.F.R. § 1271.80(d)(1) (2005).

⁵⁴ 21 C.F.R. § 1271.75(d)(1) (2005).

⁵⁵ Notably, there are exceptions to this rule. For instance, when DRT is donated by a sexually intimate partner of the recipient for reproductive use the rule does not apply. See 21 C.F.R. § 1271.90(a) (2005).

⁵⁶ 21 C.F.R. § 1271.350 (2005).

⁵⁷ See *FDA’s Guidance for Industry Announcement*, *supra* note 50, at 1.

⁵⁸ *Id.* It is important to note that according to the FDA, the Guidance for Industry “does not create or confer any rights for or on any person and does not operate to bind FDA or the public” but is rather a detailed explanation of the FDA’s expectations from tissue manufacturers with respect to their duties under the *FDA Final Donor Eligibility Rule*. *Id.*

⁵⁹ See 66 Fed. Reg. 5447, 5448 (FDA Jan. 19, 2001); *FDA’s Proposed Approach*, *supra* note 41, at 7. See also Tissue Banks: is the Federal Government’s Oversight Adequate: Hearing before the Permanent Subcomm. on Investigations of the Comm. on Governmental Affairs, 107th Cong. 106 (2001) (statement by Kathryn C. Zoon, Ph.D., Director, Ctr. for Biologics Evaluation and Research, FDA), available at http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=107_senate_hearings&docid=f:73395.pdf [hereinafter Zoon Statement] (“FDA can assure the Committee that we are committed to establishing a regulatory framework, which not only helps to ensure the safe use of human tissue for transplantation, but also . . . instills public confidence.”); *Reinventing the Regulation of Human Tissue*, *supra* note 40 (“FDA . . . has designed a new regulatory framework for cells and tissues that would protect the public health . . .”).

⁶⁰ In its Proposed Approach, the FDA described five public health and regulatory concerns, which do not lend themselves to any reading that would include the prevention of spreading of genetic diseases. See *FDA’s Proposed Approach*, *supra* note 41, at 9. Moreover, in addressing safety and efficacy aspects of human tissues having “reproductive function,” the *FDA’s Proposed*

promulgating the Final Donor Eligibility Rule, the FDA relied only on PHSA § 361,⁶¹ which grants it authority to promulgate regulations “necessary to prevent the introduction, transmission, or spread of communicable diseases”⁶² and which has no bearing on the prevention of transmission of genetic diseases.⁶³ Similarly, the FDA structured its new regulatory scheme in a way that includes DRT under a new FDA-invented category of “minimally manipulated tissue,”⁶⁴ which is subject only to regulation under the Human Tissue Regulations.⁶⁵

Interestingly, at least at one time, the FDA considered the possibility of requiring the testing of DRT for genetic diseases.⁶⁶ It is unknown why the FDA ultimately did not address this issue at all.⁶⁷ As I will show later in this Article, this exclusion of genetic aspects of DRT from the FDA’s Human Tissue Regulations was not only undesirable

Approach plainly stated that “[f]ailure of reproductive tissue generally does not have life-threatening or systemic adverse effects except for fertility per se.” *Id.* at 20. This statement does not seem to consider the possible adverse effects that genetically compromised DRT might have on DRT children.

⁶¹ See 66 Fed. Reg. 5447, 5449 (FDA Jan. 19, 2001).

⁶² See PHSA § 361 (codified at 42 U.S.C. § 264 (2008)); *infra* note 278 and accompanying text. The authority under PHSA § 361 was originally granted to the Surgeon General and was later transferred to the Assistant Secretary of Health who delegated it to the FDA. See 66 Fed. Reg. 5447, 5449 (FDA Jan. 19, 2001).

⁶³ See *infra* Part IV.A. Consequently, for example, the requirement in the Human Tissue Regulations to evaluate the donor’s medical history only applies to the *donor’s own* medical history and not to that of her family. 21 C.F.R. § 1271.3(n) (2005). Similarly, the Human Tissue Regulations do not include any requirement for testing of potential DRT donors for any genetic conditions.

⁶⁴ 21 C.F.R. § 1271.3(f) (2005). The term “minimally manipulated tissue” designates tissue that did not undergo substantial processing. Under § 1271.3(f)(2), DRT is considered minimally manipulated tissue.

⁶⁵ 21 C.F.R. § 1271.10(a)(4)(ii)(c) (2005). This diminished regulatory burden exempts DRT from additional, possibly more stringent and comprehensive, regulatory requirements under PHSA.

⁶⁶ See Letter from Diane E. Thompson, Associate Commissioner for Legislative Affairs, DHHS, to Bernice Steinhardt, Director, HEHS, GAO (Oct. 23, 1997), *available at* <http://www.gao.gov/archive/1998/he98025.pdf> (warning against the insufficiency of the FDA’s existing regulation and proposed regulatory approach with respect to the risk of introduction of genetic diseases through DRT).

⁶⁷ Notably, a report issued in 2007 by the FDA appointed Human Tissue Task Force did not even mention the issue of genetic screening and testing of DRT. See Press Release, FDA, FDA Releases Human Tissue Task Force Report (June 12, 2007) [hereinafter HTTF Report], *available at* <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108932.htm>.

from a public policy perspective but also could have been avoided had the FDA used a different set of authorities available to it to regulate DRT in general.⁶⁸

B. State Regulation

Although state law has traditionally regulated most aspects of public health and the licensing of medical personnel and facilities,⁶⁹ most states do not require any level of screening or testing of DRT for genetic diseases.⁷⁰ Roughly half of the states have some kind of regulation pertaining to the screening and testing of DRT donors for infectious diseases,⁷¹ yet only two states—New York and Ohio⁷²—impose requirements on DRT institutions to screen and test DRT for genetic risk factors.⁷³

⁶⁸ See *infra* Part IV.A.

⁶⁹ See Kathleen M. Peterson, *Federal Regulation of Artificial Insemination Donor Screening Practices: An Opportunity for Law to Co-Evolve with Medicine*, 96 Dick. L. Rev. 59, 84 (1991).

⁷⁰ See Lori B. Andrews & Nannette Elster, *Adoption, Reproductive Technologies, and Genetic Information*, 8 Health Matrix 125, 135-36 (1998); Alexander Hecht, Note, *The Wild Wild West: Inadequate Regulation of Assisted Reproductive Technology*, 1 Hous. J. Health L. & Pol'y 227, 252-53 (2001) (noting that most state statutes do not set up requirements regarding donors' medical conditions).

⁷¹ Cal. Health & Safety Code § 1644.5 (1989); Del. C. Ann. tit. 16, § 2801 (1988); Fla. Stat. Ann. § 381.0041 (2002); Ga. Code Ann. § 44-5-151 (1988); Id. Code Ann. §§ 39-3703 (1988), 39-5404 (1982), 39-5408 (1986); Id. Admin. Code §§ 16.02.07.004, 16.02.07.009; 20 Ill. Comp. Stat. Ann. §§ 2310/2310-325 (2000); Ind. Code Ann. § 16-41-14-5 (1993); 410 IAC § 25-2-2 (1992); Ky. Rev. Stat. Ann. § 311.281 (1990); La. Rev. Stat. Ann. §§ 40:1062.1 (1988), 40:1299.143 (1987); Md. Code Ann., Health – General, § 18-334(e) (1988); Mich. Comp. Laws Ann. §§ 333.9123 (1988), 333.16273 (1988), 333.20179 (1988); Mont. Code Ann. § 50-16-1008 (1989); N.H. Rev. Stat. Ann. §§ 168-B:10 (1990), 168-B:14 (1990); N.J. Stat. Ann. § 26:5C-22 (1997); N.Y. Comp. Codes R. & Regs. tit. 10, §§ 52-8.5–52-8.9 (1991); N.C. Gen. Stat. Ann. § 130A-148 (1987); Ohio Rev. Code Ann. § 3111.91 (2000); Ohio Rev. Code Ann. § 3701.246 (1989); Okla. Stat. Ann. tit. 63, § 2151.1 (1988); Or. Rev. Stat. Ann. § 677.370 (1997); 28 Pa. Code §§ 27.151 (2002), 27.21a (2002); R.I. Gen. Laws 1956, § 23-18.6.1-12 (2006); Va. Code Ann. § 32.1-45.3 (1995); 12 Va. Admin. Code §§ 5-90-240, 5-90-260 (1998); Wis. Stat. Ann. § 252.15(2)(am)(1) (1995). Notably, out of these twenty-one states, twelve (Delaware, Georgia, Illinois, Louisiana, Maryland, Michigan, Montana, New Jersey, Oklahoma, Rhode Island, and Virginia) only require the screening and/or testing of DRT for AIDS. The other twenty nine states do not seem to impose any requirement of their own on DRT institutions to screen and/or test DRT donors for diseases, whether genetic or communicable.

⁷² See *supra* note 71.

⁷³ Two more states, Idaho and Oregon, impose a duty on *semen donors* (only) not to donate if they are aware that they have “any disease or defect known by [them] to be transmissible by genes.” See I.C. 39-5404 (1982); O.R.S. § 677.370 (1997). However, the subjective element of these statutory duties seems to make them extremely difficult to enforce. Indeed, the author is

Ohio requires that in order to use semen from an anonymous donor, “[a] complete medical history of the donor, including, but not limited to, any available genetic history of the donor, [must be] obtained . . . [and] [t]he donor [must undergo] a physical examination” within one year prior to the donation.⁷⁴ In addition, practitioners using anonymously donated frozen semen must test the donor’s semen or blood using “appropriate” laboratory studies for the genetic diseases Tay-Sachs⁷⁵ and sickle-cell anemia⁷⁶ and perform karyotyping⁷⁷ of the DRT.⁷⁸ Subsequently, the DRT practitioners are explicitly required to determine whether the results of such tests “are acceptable.”⁷⁹

unaware of any case in which a donor was prosecuted or sued based on a cause of action stemming from these provisions.

An interesting question is why only New York and Ohio have relatively comprehensive regulatory schemes with respect to the genetic aspects of DRT while other states, like California—which hosts the nation’s largest DRT institution and several others—do not. Different explanations could be offered for the adoption of comprehensive regulation or lack thereof. For example, states with a significant medical industry, such as New York, could be expected to have progressive medically-related regulation. Similarly, states having a significant DRT industry, such as California and New York, could be expected to have a strong anti-regulation lobby. On the other hand, states having a strong DRT industry may strive to have stricter regulation to protect their industry from out-of-state competition. Yet, none of these possible explanations seems to provide a full explanation as to why only New York and Ohio adopted relatively comprehensive regulation of the genetic aspects of DRT while other states, such as California and Massachusetts, did not.

⁷⁴ Ohio Rev. Code Ann. § 3111.91(B)(1)(a)-(b) (2000).

⁷⁵ Tay-Sachs is a fatal genetic disorder in which harmful quantities of a fatty substance build up in tissues and nerve cells in the brain. Infants with Tay-Sachs disease appear to develop normally for the first few months of life but then suffer an ongoing deterioration of mental and physical abilities until the child’s inevitable death before the age of five. The incidence of Tay-Sachs is particularly high among people of Eastern European and Ashkenazi Jewish descent. Patients and carriers of Tay-Sachs disease can be identified by a simple blood test. Tay-Sachs disease is an autosomal recessive condition, meaning that in order to have an affected child both parents must carry the mutated gene and pass it along to the child, which has a one in four (1:4) likelihood of happening with each pregnancy. See National Institute of Neurological Disorders and Stroke, NINDS Tay-Sachs Disease Information Page, <http://www.ninds.nih.gov/disorders/taysachs/taysachs.htm> (last visited May 9, 2010).

⁷⁶ Sickle cell anemia is a disease in which the body makes sickle-shaped red blood cells (i.e. red blood cells that are shaped like a “C”) rather than normal disc-shaped blood cells. Sickle-shaped cells do not move easily through blood vessels and tend to form clumps and get stuck in the blood vessels thus blocking blood flow in the blood vessels that lead to the limbs and organs. Blocked blood vessels can cause pain, serious infections, and organ damage. Like Tay-Sachs disease, sickle cell anemia is an autosomal recessive condition. See Nat’l Heart, Lung and Blood Institute, Diseases and Conditions Index, *What is Sickle Cell Anemia?*, http://www.nhlbi.nih.gov/health/dci/Diseases/Sca/SCA_WhatIs.html (last visited Jun. 17, 2010).

⁷⁷ Karyotyping is a test to examine the number and structure of chromosomes used to diagnose numerous types of genetic diseases resulting from irregular chromosome number or structure,

While Ohio's relevant law only applies to the screening and testing of semen,⁸⁰ New York's law also applies to donated eggs, thereby making it the only state in which both sperm and oocytes⁸¹ are subject to a requirement of screening and testing for genetic diseases.⁸² The New York Regulations require practitioners to "screen and . . . assess donors for conditions that may adversely affect the quality of [DRT] or impair the recipient's and/or the offspring's health."⁸³ Under the New York Regulations, such screening must include a physical examination of the prospective DRT donor⁸⁴ as well as collection of "[a] complete medical history, both individual and family, including first-degree and second-degree relatives."⁸⁵ The donor and her family's medical history must be evaluated according to numerous criteria including: (1) the existence of major genetic disorders, autosomal or X-linked, dominant or recessive,⁸⁶ (2) a history of an occupation with increased risk of or exposure to radiation or chemicals,⁸⁷ and (3) other conditions as determined by the DRT institution.⁸⁸ If the donor's ethnic or racial group or family history indicates an increased risk of carrying⁸⁹ Tay-Sachs disease, thalassemia,⁹⁰ cystic

e.g., Down's Syndrome. See Medline Plus, Karyotyping, <http://www.nlm.nih.gov/medlineplus/ency/article/003935.htm> (last visited May 9, 2010).

⁷⁸ Ohio Rev. Code Ann. § 3111.91(B)(2)(b) (2000).

⁷⁹ Ohio Rev. Code Ann. § 3111.91(B)(2)(c) (2000).

⁸⁰ Ohio Rev. Code Ann. § 3111.91 (2000).

⁸¹ Unlike sperm banks, for scientific and technical reasons having to do with difficulties in preserving oocytes, "egg banks" essentially only mediate between recipients and potential egg donors who are willing to undergo the medical procedures necessary for harvesting their eggs. Hence, "egg banks" are not "banks" in the same sense as sperm banks, as they do not store eggs for immediate dispensing.

⁸² The New York regulations refer to "reproductive tissue" in general. See N.Y. Comp. Codes R. & Regs. tit. 10, § 52-8.5 (1991).

⁸³ N.Y. Comp. Codes R. & Regs. tit. 10, § 52-8.5(a).

⁸⁴ *Id.*

⁸⁵ N.Y. Comp. Codes R. & Regs. tit 10, 52-8.5(b).

⁸⁶ N.Y. Comp. Codes R. & Regs. tit 10, 52-8.5(b)(2).

⁸⁷ N.Y. Comp. Codes R. & Regs. tit 10, 52-8.5(b)(10). Such exposure could, supposedly increase the prevalence of genetic mutations in the donor's gametes.

⁸⁸ N.Y. Comp. Codes R. & Regs. tit 10, 52-8.5(b)(13).

⁸⁹ For the purposes of the discussion herein, a carrier is an individual who is a heterozygote—i.e., only has one copy of a recessive allele—for a disease that would only manifest itself if the individual has two recessive copies of the gene, e.g., CF, Tay-Sachs, etc.

fibrosis and/or sickle cell disease genes, he or she must be tested for these genetic conditions.⁹¹ All such test results must be made available to the donor, as well as to the practitioner who intends to use the DRT.⁹²

In addition, the New York Regulations require notification of the recipient's physician if, at the time of donation, the donor was older than forty-four in the case of a sperm donor or older than thirty-four in the case of an egg donor.⁹³ Furthermore, to avoid repeated adverse results caused by DRT use, practitioners must report the outcomes of any use, including such adverse results, to the DRT institution which must record them.⁹⁴ Finally, the DRT institution must receive informed consent from the recipient "after a physician has explained the risks and benefits of the procedure, [and] made available details of the medical history of the donor or donors."⁹⁵ New York is the *only* state with comprehensive regulation pertaining to the genetic aspects of DRT.

C. Genetic Screening and Testing of Donated Reproductive Tissue in the Courts

There are very few reported cases involving claims stemming from deficient genetic screening and testing of DRT.⁹⁶ Yet, the little case law that does exist indicates that it is extremely difficult for plaintiffs⁹⁷ to recover damages for their injuries.⁹⁸

⁹⁰ Thalassemia is a blood disorder causing the body to make fewer healthy red blood cells and less hemoglobin than normal, which could lead to mild to severe anemia. Beta thalassemia occurs when one or both genes are altered and the severity of the disease depends on how badly the gene or genes are affected. Thalassemia occurs most often among people of Italian, Greek, Middle Eastern, Asian, and African descent. Thalassemia is easily diagnosed in a blood test. *See* Nat'l Heart, Lung and Blood Inst., Diseases and Conditions Index, What Are Thalassemias?, http://www.nhlbi.nih.gov/health/dci/Diseases/Thalassemia/Thalassemia_WhatIs.html (last visited May 9, 2010).

⁹¹ N.Y. Comp. Codes R. & Regs. tit 10, 52-8.6(h).

⁹² N.Y. Comp. Codes R. & Regs. tit 10, 52-8.6(k).

⁹³ N.Y. Comp. Codes R. & Regs. tit 10, 52-8.5(d).

⁹⁴ N.Y. Comp. Codes R. & Regs. tit 10, 52-8.9(e).

⁹⁵ N.Y. Comp. Codes R. & Regs. tit 10, 52-8.8.

⁹⁶ There are, generally, very few reported court cases involving claims of deficient ART practices. Several commentators have argued that this dearth of case law in the area of ART is the result of a strong inclination of DRT institutions and practitioners to settle claims against them. *See* Karen M. Ginsberg, *FDA Approved? A Critique of the Artificial Insemination Industry in the United States*, 30 U. Mich. J.L. Ref. 823, 828 (1997) ("The rarity of litigation over unsafe artificial insemination techniques . . . may stem from the fact that most of these cases are resolved in hushed, out-of-court settlements intended to conceal the risks of [artificial insemination] from the public. . . ."); Hecht, *supra* note 70, at 233-34 (arguing that the likely explanation to the lack of litigation is the reproductive industry's preference for anonymous, out-of-court settlements which serves its attempts to avoid "negative headlines that could deter potential customers from

Plaintiffs seeking to bring a negligence claim relying on a theory of malpractice against DRT institutions or practitioners (defendants) have to show that the defendants (1) owed them a duty of care, (2) which the defendants breached, and (3) that the breach caused (4) the injury they suffered.⁹⁹ Yet, it is extremely difficult to prove all of these elements in cases involving genetically compromised DRT.¹⁰⁰ First, many courts are unwilling to recognize the existence of a duty of care to persons who did not yet exist at the time the allegedly tortious actions took place.¹⁰¹ Similarly, most jurisdictions are unwilling, conceptually, to entertain and flatly reject claims for “wrongful life,” i.e. claims that are based on the premise that tortious acts brought about the existence of a

undergoing such procedures”); Anita M. Hodgson, *The Warranty of Sperm: A Modest Proposal to Increase the Accountability of Sperm Banks and Physicians in the Performance of Artificial Insemination Procedures*, 26 Ind. L. Rev. 357, 358, 363-64 (1993) (arguing that the lack of litigation arising from improper artificial insemination is the result of “quiet, out-of-court settlements designed to prevent anxious consumers from discovering the risks involved in the procedure” as well as to protect clinicians’ professional reputations and avoid large judgments by sympathetic juries). It is likely that such a strong inclination to settle cases involving DRT institutions and practitioners would also account for the very few cases involving genetic aspects of DRT. Regardless of the reason, the few cases that actually address human reproduction (not just in the context of the genetic aspects of DRT) demonstrate not only a plethora of different approaches but also sharp inconsistencies in analysis and results between different courts (sometimes even in the same jurisdiction). See Matthew Browne, *Preconception Tort Law in an Era of Assisted Reproduction: Applying a Nexus Test for Duty*, 69 Fordham L. Rev. 2555, 2588-91, 2596-97 (2001); Hodgson, *supra* at 361-62 (suggesting a UCC-based breach of warranty claim as another possible cause of action for plaintiffs to utilize in litigation since negligence claims are often difficult to prove).

⁹⁷ The term “plaintiffs” as it is used herein refers to DRT children suffering from genetic defects resulting from deficient screening and testing of the donors of the DRT used in their conception and their legal parents.

⁹⁸ The difficulties faced by plaintiffs may well deter such potential plaintiffs from suing, which may, in turn, explain the dearth of case-law in matters involving claims stemming from deficient genetic screening and testing of DRT.

⁹⁹ See Black’s Law Dictionary 1133 (9th ed. 2009) (defining “negligence” as, *inter alia*, “[a] tort grounded in [the failure to exercise the standard of care that a reasonably prudent person would have exercised in a similar situation] . . . expressed in terms of the following elements: duty, breach of duty, causation, and damages”).

¹⁰⁰ See The President’s Council on Bioethics, Reproduction and Responsibility, The Regulation of New Biotechnologies 70-71 (2004) [hereinafter Council on Bioethics Report], available at <http://bioethics.georgetown.edu/pcbe/reports/reproductionandresponsibility/index.html>.

¹⁰¹ See Browne, *supra* note 96, at 2555-56, 2558, 2563 (arguing that existing case law illustrates that a doctor-patient relationship between the physician and a potential mother “does not automatically create a duty of care flowing from the doctor to the patient’s future child”).

severely injured person who would have otherwise (i.e., but for the allegedly wrongful acts) not existed.¹⁰²

Second, the lack of regulatory standards with respect to the duties of DRT institutions and practitioners to screen and test DRT for genetic diseases, report adverse events, etc., both at the federal and state level,¹⁰³ makes it difficult to establish the existence of a duty of care owed by such potential defendants to injured DRT children

¹⁰² Black's Law Dictionary 1752 (9th ed. 2009) (defining "wrongful-life action"). The reason for what appears to be courts' aversion to "wrongful life" claims is the result of what came to be known as the "non-identity problem." See generally C. Foster, T. Hope & J. McMillan, *Submissions from Non-Existent Claimants: The Non-Identity Problem and the Law*, 25 Med. & L. 159 (2006) (explaining how courts dismiss wrongful life claims because of the non-identity problem). A good illustration of how most courts approach wrongful life claims is the case of *Becker v. Schwartz*, 386 N.E.2d 807 (N.Y. 1978). *Becker* involved two cases: in one, a couple sued for giving birth to a child suffering from Down's Syndrome after not being informed by their doctors of the increased risk of Down's Syndrome in women over 35 years of age or about the availability of the amniocentesis test. *Id.* at 896. In the second case, a couple who gave birth to a child with polycystic kidney disease, who died five hours after birth, were allegedly told by their obstetricians that the disease was not hereditary, which was not the case. See *supra* note 8. As a result, the couple became pregnant again and gave birth to a child who also suffered from PKD and who died from it at the age of two and a half years. *Becker*, 386 N.E.2d at 896. Both couples sued for "wrongful life," claiming that had it not been for their physicians' actions and omissions they would have chosen not to give birth to or conceive their injured child. The New York Court of Appeals (the highest court of New York State) held that both complaints "failed to state legally cognizable causes of action" because "it [did] not appear that the infants suffered any legally cognizable injury." *Id.* at 811-12. With respect to the parents' causes of action, the Court of Appeals ruled that it is impossible to assess their damages since "notwithstanding the birth of a child afflicted with an abnormality . . . parents may yet experience a love that even an abnormality cannot fully dampen. To assess damages for emotional harm endured by the parents of such a child would, in all fairness, require consideration of this factor in mitigation of the parents' emotional injuries" which remains "too speculative to permit recovery." *Id.* at 814. Judge Wachtler expressed an even stricter opinion that "a doctor who provides prenatal care to an expectant mother should not be held liable if the child is born with a genetic defect" because "the physician cannot be said to have caused the defect." *Id.* at 816 (Wachtler J., dissenting in part). See also Browne, *supra* note 96, at 2558 (arguing that some courts find the policy considerations involved in a finding of a pre-conception tort to be "so momentous" that they prefer leaving such a decision to the legislature), 2588-97 (pointing at the inconsistency of analytical approaches and outcomes between different jurisdictions and courts with respect to children who "enter the world 'carrying the seal of another's fault'").

Compare this situation to other types of reproduction related causes of action which do not raise the non-identity problem such as actions for failure to provide appropriate treatment to a fetus in-utero ("regular" negligence) or failure to advise parents about the risks of having a child with birth defects. See Black's Law Dictionary 1752 (9th ed. 2009) (defining "wrongful-birth action" as "[a] lawsuit brought by parents against a doctor for failing to advise them prospectively about the risks of their having a child with birth defects.").

¹⁰³ See *supra* Parts II.A-B.

and their families.¹⁰⁴ Last, there is inherent difficulty in proving that the acts and omissions of the defendants, rather than the genetic qualities of the DRT used, were the cause of a DRT child's injuries.¹⁰⁵

Plaintiffs seeking to avoid the hardships involved in bringing a negligence action against a DRT institution might find that they have very few, if any, other possible avenues of recourse. They usually cannot sue a DRT donor who failed to report a genetic disease that eventually passed to the DRT child because the secrecy in which such private medical information is normally kept makes it very difficult to obtain.¹⁰⁶ Furthermore, almost every state excludes breach of warranty causes of action in matters involving human tissues, including cases where deficient DRT screening and testing practices would have otherwise constituted a breach of warranty by defendants.¹⁰⁷ Moreover, those plaintiffs who overcome the above-described legal hurdles, and eventually sue for damages, might encounter an overtly unsympathetic and sometimes even scornful court that might refuse (or fail) to accept the proposition that defendants' mistakes and omissions constituted negligence.¹⁰⁸ Ultimately, the genetically injured DRT children

¹⁰⁴ See Hodgson, *supra* note 96, at 361-62. As discussed *infra*, Part II.D, with the narrow exception of the states of Ohio and New York, the only standards existing in this respect are non-committing self imposed inter-industry guidelines. See Andrews & Elster, *supra* note 70, at 136. Courts, however, might not consider such standards authoritative enough to be indicative of the existence of a duty of care in malpractice claims. See *OTA's Infertility Report*, *supra* note 27, at 249. For an explanation of the inherent difficulty in proving the existence of a duty in situations where no established standard of care exists, see The Food and Drug Law Institute, *The Regulation of Human Tissues and Organs*, 46 Food Drug Cosm. L.J. 1, 150 (1990) [hereinafter *Human Tissues and Organs*] (presentation of Geoffrey R.W. Smith). Notably, while it is a "well known tort doctrine that proof of compliance with the applicable 'industry' standard will not insulate a defendant from liability when the standard itself is inadequate," the author is unaware of any case that even mentions the fertility industry's guidelines with respect to genetic screening and testing of DRT as a possible standard of care. *Lambert v. Park*, 597 F.2d 236, 239 (10th Cir. 1979).

¹⁰⁵ See *Becker*, 386 N.E.2d at 816 (Wachtler J., dissenting in part).

¹⁰⁶ See *OTA's Infertility Report*, *supra* note 27, at 249; see also *infra* Part II.C.1 (discussing *Johnson v. Superior Court*, 124 Cal. Rptr. 2d 650 (Cal. Ct. App. 2002)).

¹⁰⁷ As far back as 1993, Hodgson pointed out the shortcomings of this policy with respect to the screening and testing practices of DRT and called for its abandonment and for the application of the U.C.C. to sperm transactions. See Hodgson, *supra* note 96, at 364-86. Yet, this policy, which essentially views transactions between DRT banks and consumers as performance of "services" rather than as "sales," remains in place. See *Condos v. Musculoskeletal Transplant Found.*, 208 F. Supp. 2d 1226, 1229-30 (D. Utah 2002) ("No court has ever applied strict liability to the distribution of human tissue This is consistent with a general policy throughout the nation . . . against applying strict liability to the distribution of human tissue."); Restatement (Third) of Torts: Prod. Liab. § 19(c) and cmt. c. (1998); but see I.C. § 39-3702 (1987) (excepting paid sale of organs and tissue from the application of this rule).

¹⁰⁸ See *Harnicher v. Univ. of Utah Med. Ctr.*, 962 P.2d 67 (Utah 1998). *Harnicher* involved a "mix-up" of a chosen donor's sperm with that of another donor, leading to the birth of triplets

and their families are left to bear not only the suffering but also, at least to some extent, the costs and damages resulting from the DRT children's injuries. Two relatively recent cases exemplify many of the abovementioned problems and difficulties in litigating claims stemming from deficient genetic screening and testing of DRT donors.

1. *Johnson v. Superior Court of Los Angeles County*

In the first case exemplifying the difficulties experienced by plaintiffs suing for the mishandling of genetic aspects of DRT, Diane and Ronald Johnson bought sperm from the California sperm bank Cryobank.¹⁰⁹ A successful insemination led to the birth of a girl (Brittany) who, six years later, was diagnosed with a severe form of ADPKD.¹¹⁰ Since ADPKD is an autosomal dominant disease of which the Johnsons had no family history, they suspected that the disease was transferred to their daughter from the sperm donor.¹¹¹ After long and burdensome legal proceedings,¹¹² it was eventually revealed that

who did not resemble their recipient-father thus thwarting recipients' intention to believe and represent that the "recipient-father" is the biological father of the DRT children. The recipients sued for malpractice, alleging negligent infliction of emotional distress due to the fact that they have "suffered severe anxiety, depression, grief, and other mental and emotional suffering and distress which has adversely affected their relationship with the children and with each other." *Id.* at 68. The Utah Supreme Court chose to accept the trial court's holding that despite an expert opinion stating that plaintiffs have suffered physical symptoms as a result of their distress, they failed to convince the court that they have indeed suffered such injuries and thus cannot recover. *Id.* at 70-71. Notably, in affirming the trial court's findings, the Utah Supreme Court observed that "[plaintiffs] became the parents of three *normal, healthy children* whom the couple suggest do not look as much like [the recipient-father] as different children might have and whose blood type could not be descended from his. This result thwarted the couple's intention to believe and represent that the triplets are [the recipient-father's] biological children. *Exposure to the truth about one's own situation cannot be considered an injury and has never been a tort. Therefore, destruction of a fiction cannot be grounds for either malpractice or negligent infliction of emotional distress.*" *Id.* at 72 (emphasis added). Contrast, however, the insightful dissent of Associate Chief Justice Durham, who argued that "[the majority's conviction that the loss of an unassailable assurance that one's children carry one's genes is of negligible value] is belied by the extraordinary lengths to which thousands of people in this era will go to pursue biological parenthood" and that "[m]ost troubling. . . and unnecessary to the result of the majority opinion is its general tone of disdain for and belittlement of the nature of the suffering claimed by [plaintiffs]. This loss of genetic continuity is an important factor for the husband to discuss and to accept. No matter how well the donor is matched to the husband, this loss is real and has to be grieved over" *Id.* at 75, 77-78.

¹⁰⁹ See generally *Johnson v. Superior Court (Johnson II)*, 124 Cal. Rptr. 2d 650 (Cal. Ct. App. 2002).

¹¹⁰ According to a declaration from Brittany's doctor, she had "cysts [on her kidneys] . . . and clearly has a highly penetrant form of ADPKD. . . . [S]he [will] likely progress much more rapidly than most patients with ADPKD who don't develop cysts until their 4th or 5th decade of life." *Johnson v. Superior Court (Johnson I)*, 95 Cal. Rptr. 2d 864, 869 (Cal. Ct. App. 2000).

¹¹¹ *Johnson II*, 124 Cal. Rptr. 2d at 654.

Cryobank's personnel, who interviewed the donor, knew that he had a family medical history that indicated the existence of ADPKD.¹¹³ Still, Cryobank accepted him as a donor without further investigation to determine whether he might indeed carry the ADPKD gene, and later sold his sperm to the Johnsons without warning them about the possible genetic risks involved.¹¹⁴ Furthermore, Cryobank represented to the Johnsons that the sperm "had been tested and screened for infectious and 'reasonably detectable genetically transferred' diseases and medical abnormalities and therefore could safely be used."¹¹⁵

The Johnsons sued Cryobank and its employees for failing to disclose that the sperm they had used came from a donor with a family history of ADPKD, fraud, breach of contract and, later, also filed a motion to amend their complaint to add a claim for punitive damages.¹¹⁶ The trial court rejected the Johnsons' fraud claim, held that Brittany was not entitled to recover general damages or damages for lost earnings, and denied the Johnsons' motion to add punitive damages to their claim.¹¹⁷

On appeal, while acknowledging that there were substantial policy reasons in favor of allowing for punitive damages, the California Court of Appeals affirmed the trial court's denial of the Johnsons' motion to add punitive damages to their claim.¹¹⁸ Most importantly, the California Court of Appeals subscribed to the trial court's characterization of Brittany's claim as one for "wrongful life" and thus held that under California Supreme Court case law she was not entitled to recover general damages or damages for lost earnings.¹¹⁹ In making this decision, the Court of Appeals "recognize[d]

¹¹² The Johnsons sought to discover the identity and medical record of their donor. *See Johnson I*, 95 Cal. Rptr. 2d at 868. After a long struggle, the California Court of Appeals eventually was willing to compel the donor to appear at a deposition to answer questions and produce documents regarding his medical condition and his family's medical history, but without having to expose his identity. *See Johnson I*, 95 Cal. Rptr. 2d at 875, 878-79; *Johnson II*, 124 Cal. Rptr. 2d at 654-55.

¹¹³ *Johnson II*, 124 Cal. Rptr. 2d at 655 ("[The donor's] affirmative answers to the questions concerning the presence of kidney disease in his mother and his aunt/uncle were circled, a question mark was written next to each 'X,' and the notation 'at risk for kidney disease' was written directly above the 'X' denoting his mother's kidney disease.").

¹¹⁴ *Id.* at 654.

¹¹⁵ *Johnson v. Superior Court (Johnson II)*, 124 Cal. Rptr. 2d 650, 654 (Cal. Ct. App.2002).

¹¹⁶ *Id.* at 653-54.

¹¹⁷ *Id.* at 654-56,

¹¹⁸ *See id.* at 656-64 .

¹¹⁹ *Id.* at 664-66. The Court of Appeals explained that since it cannot be said that Defendants caused Brittany's inherited abnormalities, wherein these abnormalities were caused by the defective donated gene, under *Turpin v. Sortini*, 643 P.2d 954 (Cal. 1982) and *Andalon v.*

the harshness of the rules set forth [by the California Supreme Court] but was admittedly ‘bound’ by them.”¹²⁰ Eventually, the Court of Appeals remanded the case for further proceedings addressing only the Johnsons’ negligence and fraud claims.¹²¹ After almost another ten months of procedural back and forth in the trial court and almost seven years after the Johnsons filed their original claim, the parties settled the case for \$1,250,000, of which Brittany and her parents eventually received, after deductions of expenses and attorneys’ fees, \$750,440.56.¹²²

Perhaps the most disturbing fact in the *Johnson* case is that according to the Johnsons’ complaint, defendants may have sold to other recipients as many as 1,600 sperm specimens originating from the same donor whose sperm was used to conceive Brittany.¹²³ These specimens may have resulted in an unknown number, possibly hundreds, of DRT children who might carry the ADPKD gene originating from Brittany’s donor, develop ADPKD later in their lives, and pass the ADPKD gene along to their own offspring.¹²⁴ As mentioned earlier, this case was settled so the trial court did not proceed to address this allegation.

2. *Paretta v. Medical Offices for Human Reproduction*

Josephine and Gerard Paretta underwent IVF using an ovum from an egg donor who was represented to them as “not hav[ing] a history of mental illness or genetic diseases.”¹²⁵ Although the New York Supreme Court found that “[t]he custom and practice of the [ovum donor] program was to screen [and test] donors for various diseases

Superior Court, 208 Cal. Rptr. 899 (Cal. Ct. App. 1984), Brittany’s damages were the result of her coming into being and thus one cannot calculate them in a reasoned non-arbitrary manner.

¹²⁰ *Johnson II*, 124 Cal. Rptr. 2d at 666.

¹²¹ *Johnson v. Superior Court (Johnson II)*, 124 Cal. Rptr. 2d 650, 666 (Cal. Ct. App. 2002).

¹²² Plaintiffs’ Brief in Support of Petition Approve Compromise of Claim at 1-2, *Johnson v. Cal. Cryobank, Inc.*, No. SC043434 (Cal. Super. Ct. June 13, 2003). Of this sum, each parent received \$250,000 minus a quarter of the expenses and \$100,000 attorneys’ fees. Brittany received the remainder, \$750,000 minus \$241,862.22 for additional fees and expenses, leaving her with \$508,137.78.

¹²³ See Fourth Amended Complaint for Fraud, Negligent Misrepresentation/Suppression, Professional Negligence, Unfair Business Practices, at ¶¶ 63-64, 69, *Johnson v. Cal. Cryobank, Inc.*, No. SC043434 (Cal. Super. Ct. Apr. 2, 2003).

¹²⁴ *Id.*

¹²⁵ *Paretta v. Med. Offices for Human Reprod.*, 760 N.Y.S.2d 639, 641 (N.Y. Sup. Ct. 2003). Other details given to the Paretas about the donor included “that she was white, a second-time donor, a heterosexual, an only child of an Irish father and English mother, a Protestant, that she was five feet six inches tall, that she had dark brown hair and brown eyes, was long necked with small eyes and ears, that she had a short thin nose, dimples and high cheekbones, and that she did not have freckles.” *Id.*

and cystic fibrosis” and to “inform the patient that there was a donor or that a potential donor was a carrier,”¹²⁶ the program did not inform the Paretas that their egg donor was a carrier of cystic fibrosis. Subsequently, Mr. Paretta, who provided the sperm for the fertilization, did not undergo genetic testing to make sure that he was not a carrier of the CF gene—which he was—and the baby born from the fertilized egg (Theresa) was afflicted with CF.¹²⁷

In October 2000, the Paretas, including Theresa, sued the medical centers and units involved in their fertilization treatments for medical malpractice for failing to (1) properly screen and test the egg, (2) inform the Paretas that it tested positive for the CF gene and (3) test Mr. Paretta for the CF gene.¹²⁸ The parents also sued for emotional pain and suffering as parents of a child affected with CF and asked that punitive damages be awarded for defendants’ “egregious, grossly negligent and reckless conduct.”¹²⁹ Interestingly, the Paretas avoided the difficulties in establishing the causation element of their negligence claim by explicitly claiming that it was the defendants who “introduced the agent, which caused [cystic fibrosis] and manipulated the embryonic material [that] was implanted into Mrs. Paretta.”¹³⁰

Relying on the New York Court of Appeals decision in *Becker v. Schwartz*,¹³¹ the New York Supreme Court held that Theresa’s claims were for “wrongful birth” and denied them in their entirety.¹³² The Supreme Court further ruled:

Theresa . . . , like any other baby, does not have a protected right to be born free of genetic defects. A conclusion to the contrary permitting infants to recover against doctors for wrongs allegedly committed during in vitro fertilization would give children conceived with the help of modern medical technology more rights and expectations than children conceived without medical assistance. The law does not recognize such a distinction and neither will this court.¹³³

¹²⁶ *Id.* at 641.

¹²⁷ *Id.* at 641-42. According to the New York Supreme Court, “[f]or the first two months, Theresa was in intensive care. She underwent several surgeries and wore a colostomy bag for a month. According to plaintiffs she ‘will have to take medication for the rest of her life . . . [and] will remain under a doctor’s and/or hospital’s care for the rest of her life.’” *Id.* at 642.

¹²⁸ *Id.* at 642.

¹²⁹ *Id.*

¹³⁰ *Id.* at 643.

¹³¹ *See supra* note 102.

¹³² *Paretta v. Med. Offices for Human Reprod.*, 760 N.Y.S.2d 639, 643-46 (N.Y. Sup. Ct. 2003).

¹³³ *Id.* at 646.

The New York Supreme Court also denied the Paretas' claims for emotional distress as a result of their daughter's birth with a congenital disease.¹³⁴ Relying once again on *Becker*, the court explained:

[T]here can be no recovery for the emotional distress a parent may experience as a result of having a child with a genetic disease. There is no compelling legal authority permitting a distinction where a child has been conceived with the help of a medical technology and is born with a genetic disease. This court cannot treat the emotional distress and psychic pain suffered by parents who give birth to a sick child after in vitro fertilization any differently from that sustained by other parents. The emotional distress experienced as a result of watching a genetically diseased child suffer, horrible as it may be, is the same regardless of how the child was conceived.^[135] It unfortunately is not compensable.¹³⁶

The New York Supreme Court then went on to dismiss Mr. Paretta's claim for loss of consortium as "predicated on and inextricably interwoven with the emotional injuries suffered by Mrs. Paretta."¹³⁷ The court did hold, however, that the action did not have to be dismissed in its entirety: that "the Paretas can pursue recovery for the pecuniary expense they have borne and continue to bear for the care and treatment of their sick infant" and for punitive damages.¹³⁸ Having limited the Paretas' claims in this manner, the Supreme Court encouraged the Paretas "to vigorously pursue recovery."¹³⁹ The parties proceeded to trial and, similar to the Johnsons, after about ten more months, eventually settled their claims for \$1,300,000.¹⁴⁰

¹³⁴ *Id.* at 645.

¹³⁵ *See infra* Part II.E.

¹³⁶ *Paretta*, 760 N.Y.S.2d at 646.

¹³⁷ *Id.* at 647.

¹³⁸ *Paretta v. Med. Offices for Human Reprod.*, 760 N.Y.S.2d 639, 647 (N.Y. Sup. Ct. 2003). The New York Supreme Court also did not dismiss Mrs. Paretta's claims for compensation related to her decision to leave her job so that she could care for Theresa on a full-time basis and for the reasonable value of her services even though the court stated that it was "far from convinced of the viability of recovery of lost earnings." *Id.*

¹³⁹ *Id.* at 648.

¹⁴⁰ The case was settled before trial on Feb. 2, 2004. *See* <http://iapps.courts.state.ny.us/webcivil/FCASSearch> (index no. 122555-2000). The court records do not provide any further information about the terms of the settlement.

Leaving any critique of the *Johnson* and *Paretta* decisions aside,¹⁴¹ these cases exemplify not only how restricted the avenues of legal recourse available to injured DRT children and their families are, but also how burdensome, time consuming, expensive and legally difficult it is to recover for genetic injuries associated with DRT. Furthermore, even if we assume that the settlement amounts in the above cases were sufficient to compensate the DRT children and their families for their damages—which is highly doubtful¹⁴²—it is not clear that they are sufficiently high to create a deterrent effect that would improve the genetic screening and testing practices of DRT institutions and practitioners.

D. Self Regulation by Professional Organizations

1. The Need for Genetic Screening and Testing of Donated Reproductive Tissue Recognized

The lack of effective DRT screening and testing practices in the United States and the need for further regulation was described as early as 1979 by Martin Curie-Cohen.¹⁴³ Curie-Cohen surveyed 711 physicians who indicated that they were “likely to perform artificial insemination by [a] donor.” Of the 471 who responded to the survey, 379 reported that they actually performed artificial insemination. According to Curie-Cohen, although the risk of genetic diseases was a concern of many recipients, the survey revealed very little, if any, screening and testing of donors.¹⁴⁴ While many DRT practitioners could indicate whether the donor was part of a “select donor pool” (medical students automatically qualifying as select), screening was largely superficial. Though 96% of the physicians participating in the survey asked questions regarding donors’ family medical history, the questioning often did not entail more than asking the donor if

¹⁴¹ Some of the courts’ rationales in denying some of the plaintiffs’ causes of action are controversial while others simply are not convincing. For instance, the *Johnson* court’s decision not to allow the Johnsons to add punitive damages to their claim despite the existence of policy reasons to the contrary arguably did not allocate enough weight to what appeared to be egregious and fraudulent behavior of Cryobank’s personnel in that case. As for the *Paretta* court, in holding that “[t]he emotional distress experienced as a result of watching a genetically diseased child suffer . . . is the same regardless of how the child was conceived” the court seems to have simply ignored the fact that it was Defendants’ acts and omissions that led to the birth of Theresa with the debilitating genetic disease that brought about the Paretta’s suffering. See *supra* notes 129 and 136 and accompanying text.

¹⁴² For example, the settlement amounts do not reflect the loss of potential earnings of the respective DRT children had they not been afflicted with their debilitating genetic disorders.

¹⁴³ See Martin Curie-Cohen et al., *Current Practice of Artificial Insemination by Donor in the United States*, 300 N. Eng. J. Med. 585, 589 (1979).

¹⁴⁴ *Id.* at 585-86 (“[d]onors of semen were . . . only superficially screened for genetic diseases”).

there were any genetic diseases in the family. Also, many of the DRT practitioners expressed an underlying expectation that medical student and hospital resident would “screen themselves before donating semen.”¹⁴⁵ The survey revealed that while 94.7% of the physicians said they would reject a carrier of Tay-Sachs disease, only 1% of them said that they actually tested donors for it and only 28.8% of the physicians performed *any* biomedical test on donors in addition to blood typing.¹⁴⁶ Furthermore, the data collected by the survey revealed that many of the physicians had little understanding of genetic diseases. For example, 71.4% of the surveyed physicians said they would exclude a healthy donor who had a family history of hemophilia.¹⁴⁷ According to Curie-Cohen, only 37% of physicians surveyed actually kept records about the children born from DRT that they provided and only 30% kept any records on donors.¹⁴⁸ Curie-Cohen concluded that the screening and testing of donors for genetic diseases was inadequate and called for the establishment of a list of genetic traits that would be routinely screened and tested for, evaluation by “people trained in recognizing and evaluating genetic traits,” and a recordkeeping minimum that would include the outcome of pregnancies achieved through DRT and paternity.¹⁴⁹

Two case studies published in 1981 further illustrated the dangers of which Curie-Cohen warned. In one case, a girl was born with Tay-Sachs disease to a mother of an ethnic group in which this disease is not prevalent and the sperm of an anonymous donor, who, as it turned out, was a carrier of the disease’s gene.¹⁵⁰ In the second case, two consecutive artificial inseminations resulted in the transmission of a rare and lethal

¹⁴⁵ *Id.* at 586.

¹⁴⁶ *Id.* at 588.

¹⁴⁷ *Id.* Hemophilia is a rare bleeding disorder in which a person’s blood does not clot normally. Hemophilia is caused by a defect in one of the genes located on the X chromosome that determine how the body makes blood clotting factors VIII and IX. Females have two X chromosomes, while males have one X and one Y chromosome. Since only the X chromosome carries the genes related to clotting factors a male who has the abnormal gene on his X chromosome will have hemophilia while a female must have the abnormal gene on both of her X chromosomes to have hemophilia, which is very rare. This also means that while healthy females might be carriers of a hemophilia allele, males cannot possibly be carriers of this allele without actually having the disease. *See generally* National Heart, Lung and Blood Institute Diseases and Conditions Index, What is Hemophilia?, http://www.nhlbi.nih.gov/health/dci/Diseases/hemophilia/hemophilia_what.html (last visited May 9, 2010).

¹⁴⁸ Curie-Cohen, *supra* note 143, at 588.

¹⁴⁹ *Id.* at 589.

¹⁵⁰ William Johnson et al., *Artificial Insemination by Donors: the Need for Genetic Screening. Late-Infantile GM2-Gangliosidosis Resulting From This Technique*, 36 N. Eng. J. Med. 572, 755 (1981).

genetic disease to two siblings conceived from the sperm of a single donor.¹⁵¹ Tragically, the second insemination, leading to the birth of the second afflicted child, had already taken place by the time the doctors diagnosed the lethal disease in the older sibling. Both siblings died very young—at sixteen and three months, respectively—as a result of the genetic disease they inherited from the sperm donor.¹⁵²

During the 1980s, these data prompted more calls for regulation of DRT in general and their genetic aspects in particular. A 1988 survey of the former Office of Technology Assessment (OTA) revealed that donor screening and testing practices were “quite varied.” For example, while many physicians routinely rejected potential donors for such traits as “psychological immaturity,” “less than a high school education” and “less than average height,” only about half of the physicians tested any of their potential donors for any genetic diseases.¹⁵³ The OTA 1988 Survey further revealed that only 44% of the physicians performing AI required screening and testing for genetic diseases for which the potential donors were at high risk.¹⁵⁴ The Survey found that while all of the fifteen DRT institutions that responded to the survey did *some* testing of varying nature and extent, two of the fifteen DRT banks reviewed did not test for ethnically prevalent genetic diseases such as Tay-Sachs, sickle-cell anemia and thalassemia.¹⁵⁵ In addition, the Survey disclosed that only two-thirds of the DRT banks *ever* rejected a donor for having a family history of a serious genetic disease or for being over forty years of age.¹⁵⁶

Another OTA report published in 1988 further revealed that only 20% of the physicians who regularly performed AI indicated that a family history of genetic disease would prompt them to require further genetic testing of a potential donor and only 18% indicated they would do so with a potential donor from a high risk ethnic group.¹⁵⁷ The OTA 1988 Infertility Report concluded that “genetic testing is not routine for donors, including those in higher than average risk groups.”¹⁵⁸

¹⁵¹ David Shapiro & Raymond J. Hutchinson, *Familial Histiocytosis in Offspring of Two Pregnancies after Artificial Insemination*, 36 N. Eng. J. Med. 573, 757 (1981). Shapiro and Hutchinson called for extreme caution in using sperm from the same donor for artificial insemination when a child conceived from the sperm is afflicted with an unknown disorder. *Id.* at 759.

¹⁵² *Id.* at 757-58.

¹⁵³ See OTA 1988 Survey, *supra* note 14, at 9, 33-35, 66-70.

¹⁵⁴ *Id.* at 9.

¹⁵⁵ *Id.* at 11, 68.

¹⁵⁶ *Id.* at 67. Like Curie-Cohen, the 1988 OTA Survey also found that 49-63% of the physicians performing AI would reject a healthy potential donor for having a family history of X-linked genetic diseases although it would be impossible for such a donor to transmit those defects to their offspring. *Id.* at 10; see also *supra* note 147.

¹⁵⁷ See OTA's Infertility Report, *supra* note 27, at 35.

¹⁵⁸ *Id.*

The OTA's 1988 reports proved to be a benchmark in the calls for the regulation of DRT in general, and their screening and testing in particular.¹⁵⁹ Later commentators have also recognized the importance of genetic screening and testing of DRT donors and their evaluation by genetics specialists.¹⁶⁰ Ultimately, it was not government authorities who rose to the challenge but rather professional organizations, such as the American Society for Reproductive Medicine (ASRM) and the American Association of Tissue Banks (AATB).

2. The ASRM Guidelines for Gamete and Embryo Donation

The ASRM Guidelines¹⁶¹ set out to "provide the latest recommendations for evaluation of potential sperm, oocyte, and embryo donors, incorporating recent information about optimal screening and testing for . . . genetic diseases."¹⁶² With respect to semen donation, the ASRM Guidelines determine that the "main qualities to seek in selecting a donor . . . are an assurance of good health status and the absence of genetic abnormalities . . . [and] [t]he donor should be . . . ideally, less than 40 years of age,"¹⁶³ oocyte donors should preferably be between the ages of 21-34.¹⁶⁴ The ASRM Guidelines specify that potential sperm and egg donors should undergo genetic screening

¹⁵⁹ See Marwick, *supra* note 27, at 1339 (describing [then] Senator Albert Gore's criticism of the FDA's non-regulation of AI in light of the *OTA 1988 Survey*).

¹⁶⁰ See, e.g., Lisa Kump et al, *The Importance of Genetic Screening for Oocyte Donors*, 78 Fertility & Sterility S43, S43 (2002) (describing the genetic screening and testing of 607 prospective egg donors, which resulted in the exclusion of 71 of them, i.e., more than 12%, and concluding that genetic screening of prospective egg donors that included detailed family history and testing for a number of diseases should be encouraged "to assure optimal short-term and long-term outcomes for pregnancies achieved through . . . donation"); Rubens L.C. Tavares et al., *The Value of Genetic Screening of Oocyte Donors Couples*, 80 Fertility & Sterility S138, S138 (2003) (reporting that genetic screening of prospective egg donors resulted in the exclusion of more than 20% of the prospective donors for such reasons as having sickle cell anemia and having prior children with mental retardation); Robert Wallerstein et al., *Genetic Screening of Prospective Oocyte Donors*, 70 Fertility & Sterility 52, 52 (1998) (reporting the exclusion of eight out of 73 egg donor candidates (11%) due to "serious genetic findings" and concluding that "[a] thorough genetic evaluation, including a history and laboratory [test]ing, is essential to any oocyte donation program to maximize positive outcomes").

¹⁶¹ See generally The Practice Comm. of the Am. Soc'y for Reproductive Med. and the Practice Comm. of the Soc'y for Assisted Reprod. Tech., *2006 Guidelines for Gamete and Embryo Donation*, 86 Fertility & Sterility S38 (2006) [hereinafter *ASRM Guidelines*].

¹⁶² *Id.* at S38.

¹⁶³ *Id.* at S40 § VI.A.1-2.

¹⁶⁴ If a prospective donor is older than 34, the Guidelines require that the donor's age be revealed to the recipient as part of the informed consent discussion concerning the possible effect of donor age on genetic risks. *Id.* at S44 § VI.B.3, 5.

and testing for heritable diseases, including carrier status for CF in all donors and other genetic testing as indicated by the donor's ethnic background and in light of the family history.¹⁶⁵ The ASRM Guidelines also set an explicit "minimum" standard for genetic screening and testing of DRT donors, according to which donors and their first degree relatives (parents, siblings and children) must not have (1) any major Mendelian disorder, such as Huntington's disease;¹⁶⁶ (2) any major functional or cosmetic malformation of complex cause, such as spina bifida¹⁶⁷ or heart malformation;¹⁶⁸ or (3) any significant familial disease with a major genetic component.¹⁶⁹ The ASRM Guidelines further require that donors must not carry any known karyotypic abnormality that might result in chromosomally unbalanced gametes and that donors should be tested for carrier status of CF and genetic disorders for which they are in a high-risk group.¹⁷⁰

3. The American Association of Tissue Banks (AATB) Standards for Tissue Banking

Like the ASRM Guidelines, the AATB Guidelines¹⁷¹ are meant to "prevent disease transmission"¹⁷² and preliminarily require compliance with any and all applicable

¹⁶⁵ See *id.* at S40 § VI.B.2 (sperm donors); see also *id.* at S44 §§ VI.B.7, VI.C.1 (egg donors). Notably, the ASRM Guidelines clarify that as new tests for genetic risk factors become available, "every effort should be made" to have samples of sperm that are cryopreserved tested in accordance with the new standards. *Id.* at S42 § IV.B.6.d.

¹⁶⁶ Huntington's disease (HD) results from a genetically programmed degeneration of brain cells in certain areas of the brain which causes uncontrolled movements, loss of intellectual faculties, and emotional disturbance. HD is an autosomal dominant disease, which means that if a child inherits the HD gene he or she will develop the disease. Each child of an HD parent has a 50-50 chance of inheriting the HD gene. A person who inherits the HD gene will sooner or later develop the disease. See Nat'l Inst. of Neurological Disorders and Stroke, Huntington's Disease Information Page, <http://www.ninds.nih.gov/disorders/huntington/huntington.htm> (last visited May 9, 2010).

¹⁶⁷ Spina bifida (SB) is a disorder involving incomplete development of the brain, spinal cord, and/or their protective coverings caused by the failure of the fetus's spine to close properly during the first month of pregnancy. Infants born with SB sometimes have an open lesion on their spine where significant damage to the nerves and spinal cord has occurred. See Nat'l Inst. of Neurological Disorders and Stroke, Spina Bifida Information Page, http://www.ninds.nih.gov/disorders/spina_bifida/spina_bifida.htm (last visited May 9, 2010).

¹⁶⁸ Notably, the ASRM Guidelines acknowledge that "'major' is a matter of judgment." *ASRM Guidelines*, *supra* note 161, at Appendix A S50.

¹⁶⁹ *Id.*

¹⁷⁰ *Id.*

¹⁷¹ See generally Am. Ass'n of Tissue Banks, Standards for Tissue Banking (10th ed. 2002) [hereinafter *AATB Guidelines*].

statutory and regulatory standards.¹⁷³ The AATB Guidelines state that donor suitability should be evaluated based upon medical, social and sexual history,¹⁷⁴ physical examination and laboratory tests.¹⁷⁵ The evaluation should include “any history of chemical and/or radiation exposure as well as family medical history and genetic background;”¹⁷⁶ specifically, it should entail an evaluation by a person knowledgeable in clinical genetics of at least three generations of the donor’s family history.¹⁷⁷ The AATB Guidelines set an age limit of forty years for semen donors and thirty-five years for egg donors¹⁷⁸ and require that “[a]ny condition in a prospective donor or donor’s family history that would pose a risk of producing an offspring with a genetic disease or defect greater than the risk in the general population shall disqualify him/her as a donor.”¹⁷⁹ The Guidelines further explicitly require that if there is an indication of a risk of Tay-Sachs disease, thalassemia, sickle cell anemia or CF in the donor’s medical history, family history or ethnic background, the donor should be tested for such conditions.¹⁸⁰

Interestingly, although the AATB Guidelines use compulsory language, their sole sanction for non-compliance is withdrawal of accreditation “upon a determination . . . that significant non-compliance, such as repeated violations, one or more egregious violations, uncorrected violations or deliberate falsehoods, have occurred.”¹⁸¹

¹⁷² *Id.* at iv.

¹⁷³ *Id.* at 1 § A1.000.

¹⁷⁴ According to the AATB Guidelines, the medical history should be reviewed by a “trained individual” and include previous medical records, test results, and conversation with attendant medical staff. *Id.* § D4.230.

¹⁷⁵ *Id.* at 31 § D4.100.

¹⁷⁶ *Id.* at 34 § D4.220.

¹⁷⁷ *AATB Guidelines*, *supra* note 171, at 35 § D4.221.

¹⁷⁸ *Id.* at 45-46 § D4.400.

¹⁷⁹ *Id.*

¹⁸⁰ *Id.*

¹⁸¹ *Id.* at iv-v, 1 § A1.000.

4. Contemporary Genetic Screening and Testing Practices of DRT Institutions and Adherence to the Professional Guidelines

Relatively recent studies indicate that not much has changed since the 1980s with respect to the genetic screening and testing practices of DRT.¹⁸² According to a study published in 2007, the four participating DRT institutions tested potential donors for blood type, Rh factor, drugs and sexually transmitted infections, gave them psychological evaluations and required them to prepare a detailed family health history for three generations.¹⁸³ Yet, none of the DRT institutions had a requirement for any mandatory genetic testing and not even all of them had the donors' medical history evaluated by a genetics specialist who, presumably, could have indicated whether further testing was necessary.¹⁸⁴

Another survey attempted to determine how the practices of DRT institutions which are members of the AATB vary from the AATB Guidelines.¹⁸⁵ According to this survey, while all sixteen sperm banks that responded¹⁸⁶ required prospective donors to provide their medical and family history and undergo a physical examination, only thirteen (81% of the DRT institutions) tested men of ethnic risk groups for Tay-Sachs disease, sickle cell anemia and thalassemia; only four (25%) tested all donors for CF; only eight (50%) reported they would test for CF even if there was a positive family history of the disease;¹⁸⁷ and only six had a genetic professional on staff.¹⁸⁸ Amazingly, three DRT institutions (19%) rejected prospective sperm donors based on a positive family history of color blindness and seven banks (44%) did so with a family history of

¹⁸² See, e.g., U.S. General Accounting Office (GAO), *Human Tissue Banks: FDA Taking Steps to Improve Safety, but some Concerns Remain* 14-15 (1997) [hereinafter *GAO 1997 Report*] (discussing non-compliance of AATB members with the AATB Guidelines).

¹⁸³ Rene Almeling, *Selling Genes, Selling Gender: Egg Agencies, Sperm Banks, and the Medical Market in Genetic Material*, 72 Am. Soc. Rev. 319, 324, 327-28 (2007) (discussing how the social process of bodily commoditization varies based on sex and gender in the context of egg and sperm donations).

¹⁸⁴ *Id.* at 328.

¹⁸⁵ See Conrad, *supra* note 10, at 298.

¹⁸⁶ Notably, another twenty-one DRT institutions chose not to participate in the survey. According to Conrad, those DRT institutions that participated in the survey "were primarily large-volume, private, nationally based commercial cryobanks, in contrast to regional cryobanks serving a limited population." See *id.* at 299. Presumably, the non-participating DRT institutions were in even poorer compliance with the AATB Guidelines than the participating DRT institutions.

¹⁸⁷ See *id.* at 298.

¹⁸⁸ *Id.*

hemophilia.¹⁸⁹ The survey's conclusion was that "[c]onsiderable differences exist among semen bank practices in accordance with guidelines published by national agencies."¹⁹⁰

A similar survey focusing on the compliance of 159 oocyte donation programs with the ASRM Guidelines revealed "considerable variability" in the practices of screening and testing for genetic disorders.¹⁹¹ According to this survey, only 72% of the oocyte donation programs tested donor candidates from ethnic groups at higher risk for sickle cell anemia and only 77% did so with respect to Tay-Sachs disease.¹⁹² The survey had several even more alarming findings, e.g., that only 62% of the participating programs said they would exclude applicants with first-degree relatives who had ADPKD.¹⁹³ In other words, more than a third of the programs that took the survey confirmed that they would knowingly expose babies born from eggs originating from donors who had a first degree relative with ADPKD to a risk of 25% of developing ADPKD.¹⁹⁴ The survey's conclusion was that while most programs followed ASRM Guidelines, "a significant minority . . . do[] not use well-established [genetic] . . . tests."¹⁹⁵ The findings of the abovementioned surveys are underscored by the fact that not all DRT institutions participate in professional accreditation programs, such as those of the AATB and ASRM.¹⁹⁶

¹⁸⁹ *Id.* at 300. Like hemophilia, color blindness is an X-linked recessive disorder. As explained above, such rejection could have no medical/genetic basis. *See supra* note 147.

¹⁹⁰ Conrad, *supra* note 10, at 300.

¹⁹¹ Vivian Lewis et al., *Survey of Genetic Screening for Oocyte Donors*, 71 *Fertility & Sterility* 278, 278 (1999).

¹⁹² *Id.* at 279.

¹⁹³ *Id.* at 280 (Table 1). Similarly, only 76% of the programs reported they would do so in the case of Huntington's disease. *Id.* For a discussion of Huntington's disease, see *supra* note 166.

¹⁹⁴ *See supra* note 8 (discussing ADPKD). With only 62% of the programs taking the survey confirming that they would exclude applicants with first-degree relatives who had ADPKD, the implication is that 38% of the programs *would not exclude applicants with first-degree relatives who had ADPKD*. This means that these programs would actually include in their DRT donation programs individuals with first-degree relatives having ADPKD. Statistically speaking, this would mean that these egg donation programs would knowingly sell eggs from donors having a 50% chance of having ADPKD themselves. Since a child has a 50% chance of getting the ADPKD gene from a parent having this gene, children born from eggs originating from such donors have a 25% chance (50% of 50%) of having the ADPKD gene themselves. *See supra* note 8.

¹⁹⁵ Lewis et al., *supra* note 191, at 280-81.

¹⁹⁶ For example, out of an estimated 400 or more tissue banks existing in the United States in the early 1990s, only forty were inspected and accredited by the AATB. *See* Barbara Indech, *The International Harmonization of Human Tissue Regulation: Regulatory Control Over Human Tissue Use and Tissue Banking in Select Countries and the Current State of International Harmonization Efforts*, 55 *Food & Drug L.J.* 343, 348 (2000). In 2003, out of 115 sperm banks

Importantly, by 2005 the FDA was aware of the non-uniform compliance of DRT institutions with self-imposed professional standards. According to the FDA Final Donor Eligibility Rule, only 80% of the examined institutions providing ART services adhered to professional standards and guidelines.¹⁹⁷ Moreover, while the FDA estimated that compliance of tissue banks with professional standards of donor screening and testing neared 100% for several types of tissues, it recognized that “facilities handling reproductive tissue [were] the primary exception to this finding” and that most sperm banks did not follow voluntary industry standards.¹⁹⁸ The FDA also acknowledged that only a small percentage of the sperm banks surveyed were members of the AATB and followed its Guidelines on screening and testing.¹⁹⁹

In conclusion, despite the existence of professional guidelines setting clear requirements for genetic screening and testing of DRT, effective enforcement mechanisms and deterring sanctions are lacking. As such, compliance by DRT institutions with such guidelines is varied and depends on the level of commitment of each individual DRT institution. Persistent findings of non-compliance with self-imposed professional guidelines since the 1990s indicate that this picture of non-uniform

nationwide, only 11 were accredited by the AATB. See Gail Schmoller Philbin, *Web of Conception; Couples Turning to Internet Sites to Secure Donated Sperm*, Chicago Tribune, Aug. 20, 2003, at C1. Similarly, the GAO 1997 Report disclosed that only approximately one-third of the reproductive laboratories in the United States existing at that time were accredited by the ASRM. See *GAO 1997 Report*, *supra* note 182, at 10. The reality of non-participation in professional regulation of DRT is easily noticeable upon browsing through internet websites of DRT banks: out of about a dozen internet websites of sperm banks visited by the author, while all of the sperm banks boasted the “quality” of their DRT, only one sperm bank clearly indicated that the bank is a member of the AATB. Notably, this fact is a further indication of the low enforceability of professional guidelines on DRT institutions. The fact that many DRT institutions are not members of the ASRM and AATB is also an indication that DRT institutions might not be concerned that such non-membership would have a detrimental effect on their ability to do business, which, in turn, reflects on the ability of the ASRM and AATB to enforce their guidelines on those DRT institutions that *are* members. In other words, the fact that there are, apparently, many DRT institutions that are not even members of or accredited by the AATB and ASRM is an indication that non-compliance with the guidelines of such professional organizations is of little or no concern to DRT institutions and that the potential implications of such non-compliance (if any) carry little (if any) deterrent effect.

¹⁹⁷ The FDA’s survey covered 110 sperm banks and 400 establishments providing ART services. See *FDA Final Donor Eligibility Rule*, *supra* note 24, at 68654. This data was part of the FDA’s reasoning for the need for federal regulation of DRT institutions with respect to communicable diseases.

¹⁹⁸ *Id.* at 29817-18.

¹⁹⁹ *Id.*

compliance is not transitory and is unlikely to change without government intervention.²⁰⁰

E. Why the Current Regulation of Genetic Aspects of Donated Reproductive Tissue is Insufficient and the Need for Additional Protection of DRT Recipients and DRT Children

1. The Insufficiency of Self-Regulation

Evidently, and as recognized by fertility professionals and the FDA, self-regulation is insufficient for ensuring the health and welfare of DRT children and their families.²⁰¹ There is persistent data showing that a significant portion of DRT institutions are not even members of the ASRM or AATB.²⁰² Even those establishments that are members of ASRM and AATB often do not adhere to the professional guidelines set by these organizations,²⁰³ and there is significant variance in genetic screening and testing

²⁰⁰ See also Conrad, *supra* note 10, at 301 (pointing out that despite more than a decade (at that time) of proposals for genetic screening and testing of DRT, no changes have taken place in the practices of DRT institutions).

²⁰¹ See also 66 Fed. Reg. 5452 (FDA Jan. 19, 2001) (expressing the FDA's view that, in the context of communicable diseases, "extending regulation to reproductive cells and tissues will remedy a significant gap in oversight. Although we recognize the value of professional efforts to self-regulate, and of regulatory efforts of other agencies and the States, we disagree that these piecemeal, often voluntary, efforts are adequate"); Cohen, *supra* note 23, at 352 (expressing doubts regarding the ability of the medical profession to effectively self-regulate the field of ART); Ginsberg, *supra* note 96, at 829 (arguing that the lack of established mechanisms to police compliance with professional guidelines causes irregular compliance); Jennifer L. Rosato, *The Children of ART: Should the Law Protect them from Harm?*, 57 Utah L. Rev. 57, 62-63 (2004) ("Although there is some self-regulation of fertility practices through professional medical organizations, the system is not well-equipped to curb harmful or unethical practices.").

Notably, some commentators have expressed concerns that the current regulation of genetic aspects of DRT also fails to recognize and promote the interests and well-being (not only the safety) of DRT children and their families as well as those of society as a whole. See Council on Bioethics Report, *supra* note 100, at 195; Erik Parens & Lori Knowles, *Reprogenetics and Public Policy—Reflections and Recommendations*, Hast. Ctr. Rep., July-August 2003, at S3, S7-S9 (2003).

²⁰² See *supra* note 196 and accompanying text. This non-compliance with self regulation requirements was apparently one of the rationales for the FDA's creation of the Human Tissue Regulations. See also 66 Fed. Reg. 5450 (FDA Jan. 19, 2001) ("[FDA has] considered the efforts of professional organizations and we will continue to do so as we implement the new regulations. However, not all [tissue] establishments belong to or are accredited by such groups and voluntary programs are not enforceable.").

²⁰³ See GAO 1997 Report, *supra* note 182, at 14-15; ISLAT Working Group, *supra* note 2, at 651 ("Despite the existence of voluntary guidelines . . . abuses continue to occur"); Human

standards between DRT institutions.²⁰⁴ The resultant risks of this reality are further exacerbated by the general vulnerability of DRT recipients. In particular, many DRT recipients do not possess the medical or scientific background necessary to enable them to “ask the right questions” or properly evaluate some of the risks involved.²⁰⁵

Moreover, the current scheme of self-regulation relies primarily on the diligence and integrity of practitioners as well as on donors volunteering pertinent information about their medical history and that of their families. However, practitioners operate in a highly competitive market that creates strong financial incentives that do not necessarily coincide with the best interest of DRT recipients and DRT children.²⁰⁶ Potential donors’ answers regarding their medical history and that of their families are also often insufficient to properly evaluate the genetic risks they might pose.²⁰⁷ Furthermore, the financial benefit to donors accompanied by the absence of a clear legal duty to accurately

Tissues and Organs, *supra* note 104, at 56 (presentation of Armand M. Karow) (“Perhaps the most important problem here is the inability of private groups to compel compliance . . . voluntary standards are just that—voluntary.”). In addition, the enforcement mechanisms of professional societies are ineffective and the only penalty for non-compliance is revocation of membership. See Daar & Brzyski, *supra* note 15, at 1704 (“[D]ata suggest the majority of sperm banks and egg donor agencies do not follow the established screening protocols . . . Even in centers that did report testing, most did not fully follow the guidelines set forth by the American Society for Reproductive Medicine.”); Alicia Ouellette et al., *Lessons Across the Pond: Assisted Reproductive Technology in the United Kingdom and the United States*, 31 Am. J.L. & Med. 419, 430 (2005) (“[T]here are no legal consequences for non-accredited U.S. programs . . . there is also ‘no consumer-recognized seal of approval or standard symbol that conveys that any minimum standards of quality have been met.’”); Rosato, *supra* note 201, at 66-67.

²⁰⁴ See, e.g., The N.Y. State Task Force on Life and the Law, Assisted Reproductive Technologies, Analysis and Recommendations for Public Policy 251 (1998) (“The type of family history information that would disqualify a prospective egg donor varies considerably at programs in New York State.”); Daar & Brzyski, *supra* note 15, at 1704 (“Current use of genetic screening by sperm and egg donor enterprises is best described as inconsistent.”).

²⁰⁵ See Julie Marquis, *Gift of Life, Questions of Liability*, Los Angeles Times, Aug. 9, 1997, at A1 (describing the *Johnson* Case and referring to Diane Johnson’s admission that she “didn’t even know what to ask”); see also Rosato, *supra* note 201, at 71 (arguing that future parents tend to want to achieve pregnancy as quickly as possible thereby making them more prone to take unnecessary risks), Meena Lal, Comment, *The Role of the Federal Government in Assisted Reproductive Technologies*, 13 Santa Clara Computer & High Tech. L.J. 517, 535 (1997) (arguing that “consumers” of IVF treatments, are often too emotionally involved to “maintain an objective and cautious stance toward the practices of institutions and individuals providing the service”).

²⁰⁶ See, e.g., Rosato, *supra* note 201, at 71-72 (describing the strong incentives fertility practitioners have to provide couples with a pregnancy as quickly as possible).

²⁰⁷ See GAO 1997 Report, *supra* note 182, at 37 (disclosing a study conducted by one tissue bank which found that 9.8% of 1,000 donors whose families provided a medical history that did not indicate genetic risk factors were rejected upon testing or autopsy).

disclose such information²⁰⁸ might render the current screening practices—which rely mostly on questioning of potential donors—unreliable because they create an incentive for potential donors to hide negative medical facts about themselves and their families.²⁰⁹ As a result, a significant number of the many thousands of children born every year from DRT are exposed to a heightened risk of having severe genetic diseases which could have been avoided through proper genetic screening.

2. The Inadequacy of the Relief Afforded by Courts

One would have expected that once the risks embedded in the current system came to bear on a particular child, such individual born from genetically defective DRT would be able to obtain appropriate relief in court. Yet, the few published cases pertaining to genetic injuries of children born from DRT raise significant doubts as to the adequacy of the court system for providing sufficient and timely remedies to such children and their families or to create the deterrent effect needed in order to avoid similar future injuries.²¹⁰

First, in order to make a viable claim, injured DRT children and their families have to trace their maladies back to the acts and omissions of a DRT institution—a legal and scientific feat in and of itself.²¹¹ Second, as demonstrated by the *Johnson* and *Paretta* cases, the causes of action available to plaintiffs in such matters are limited²¹² and difficult to establish.²¹³ Finally, to the extent that *Johnson* and *Paretta* are representative of cases involving injuries caused by genetically defective DRT, the

²⁰⁸ Only two states explicitly require potential donors to disclose relevant medical information fully and accurately. *See supra* note 73.

²⁰⁹ *See* Curie-Cohen, *supra* note 143, at 588.

²¹⁰ Annas, *supra* note 22, at 936 (arguing that the courts' deference to the contractual relationship between DRT manufacturers and parent-consumers is inadequate due to its failure to acknowledge and protect underlying interests of children, parents and society); Amy Shelf, *A Need to Know Basis: Record Keeping, Information Access and the Uniform Status of Children of Assisted Conception Act*, 51 Hastings L.J. 1047, 1067 (2000) (raising doubts as to the sufficiency of tort claims to create an incentive for DRT manufacturers to perform genetic testing and compile medical records).

²¹¹ *See supra* Part II.B (discussing this issue); *see also supra* note 112 and accompanying text.

²¹² The current law, at least in California and New York, does not provide injured DRT children with effective means of suing for their injuries. *See supra* Part II.C; *see also* Annas, *supra* note 22, at 938 (arguing that the current regulatory framework is a “bad way to protect children” because it focuses on “provid[ing] the adults involved with what they want” rather than making the children born the first priority).

²¹³ *But see* Browne, *supra* note 96, at 2608-09 (suggesting a different approach to establishing liability of DRT manufacturers that would circumvent some of the problems and hardships inherent to the current legal framework).

settlement amounts in such cases are arguably too low to create a real incentive for DRT institutions to improve their genetic screening and testing practices.²¹⁴

Even if we ignore the fact that lawsuits impose significant financial burdens that not everyone is capable of bearing, judicial remedies are, by definition, case-specific and retrospective and, therefore, too late for the genetically injured child and her family; by the time of the trial, the child and her family have already experienced pain and suffering and will live with the consequences of the genetic injury for the rest of their lives.²¹⁵ Additionally, because the genetic risks to DRT children might manifest many years after the treatment took place, medical malpractice litigation may not be an effective venue for obtaining “real time” quality control.²¹⁶

3. DRT Recipients and DRT Children are Entitled to and It Is Desirable that They Have Additional Legal Protection

The *Paretta* court’s proposition that DRT children’s injuries are not compensable where similar injuries of non-DRT children would not be compensable²¹⁷ is unjustifiable and ignores significant differences between the circumstances of conception and gestation of DRT and non-DRT children. First, the conception of DRT children always involves a third party—a “middleman”—that normally makes certain representations, both direct and implied, to the recipients regarding the DRT, which often create certain expectations—reasonable or not—regarding the characteristics of the DRT and future

²¹⁴ Since *Johnson* and *Paretta* are the only two reported cases available, it is difficult to make an inference from them as to all matters involving injuries resulting from genetically defective DRT. Still, *Johnson* and *Paretta* may be indicative of how plaintiffs in such cases perceive their chances in court and therefore their leverage in settlement negotiations. See also Hecht, *supra* note 70, at 258 (“[The] unfavorable trial conditions force plaintiffs to settle for less, while clinics are not required to improve the safety of their facilities.”); Hodgson, *supra* note 96, at 364 (observing that while settlement amounts in cases involving defective sperm ensure minimal compensation, they do little to compel sperm banks and physicians to take action that would circumvent similar defects in the future).

²¹⁵ See Cohen, *supra* note 23, at 353 (arguing that the court system does not provide an adequate method of regulation in the area of ART, where it is necessary to avert permanent harm in advance); Ginsberg, *supra* note 96, at 841 (arguing that litigation is an inadequate enforcement mechanism because it is retrospective, deals with injuries of individual parties, results in ad-hoc policy limited to case-specific circumstances and generally fails to deter abuses in the AI industry); Hodgson, *supra* note 96, at 364 (observing that once a genetic disease has manifested in a child, it is difficult to compensate for the pain and suffering resulting from the injury); Shelf, *supra* note 210, at 1067 (arguing that tort remedies, by nature, are insufficient to recover lost genetic and medical information).

²¹⁶ See ISLAT Working Group, *supra* note 2, at 651.

²¹⁷ See *supra* note 136 and accompanying text.

DRT child.²¹⁸ Second, in assisted reproduction, gametes go through an “in-vitro stage,” a period of time in which they are external to the donor and recipient’s body alike. This period of time, even if short, creates a unique opportunity to manipulate the DRT or subject it to selection that is meant to achieve favorable results in the future DRT child²¹⁹ and which, as before, often creates expectations regarding the future DRT child and her genetic makeup. Thus, the *Paretta* court was mistaken in its refusal to distinguish between assisted and non-assisted reproduction, especially in the context of DRT.²²⁰

Furthermore, the proposition that parents cannot have reasonable expectations that their DRT children will not suffer from genetic diseases²²¹ flies in the face of reality as DRT recipients often have an underlying—many would say justified—expectation that their DRT children would have significantly lower chances of having genetic diseases than non-DRT children.²²² In fact, many DRT recipients seek to use DRT precisely *because* they wish to avoid the risk of their child having a genetic disease and ensure “high quality” genetic traits.²²³ Thus, denying DRT recipients the assurance of genetic

²¹⁸ The third party is also usually well informed and aware of the medical risks typical to the use of DRT. This makes the representations of the third party—normally a medical practitioner—credible and therefore more likely to be relied upon. Unsurprisingly, it is that “third party” that is usually being sued. Arguably, parties choosing to procreate in a non-assisted manner have, at least hypothetically, sufficient opportunity to inform each other and become informed with respect to their respective medical condition and genetic makeup.

²¹⁹ E.g., manipulation of sperm to select the sex of the future child, picking sperm from a donor who resembles the future father to maintain semblance between him and the future DRT child and more.

²²⁰ Rather than refuse to distinguish between assisted and non-assisted reproduction, the *Paretta* Court should have determined whether the DRT institution had a duty toward the recipients and DRT child based on the particular circumstances of the case and regardless of the question of comparability to non-assisted reproduction. The court should have left the comparability question to later cases addressing the issue from the non-assisted reproduction perspective, i.e., whether children conceived *via unassisted reproduction* could receive the same type of relief as children conceived *via assisted reproduction*.

²²¹ See *supra* notes 134-136 and accompanying text.

²²² See, e.g., Orenstein, *supra* note 10, at 39 (“[Future parents seeking to use DRT to achieve a pregnancy instead of adopting a child] wanted the opportunity to hand-pick a donor’s genes rather than gamble on a birth mother’s and father’s.”); John A. Robertson, *Procreative Liberty in the Era of Genomics*, 29 Am. J.L. & Med. 439, 460 (2003) (“[U]sing gamete and embryo selection technologies to ensure healthy offspring [is] of great importance to individuals.”); Amy Harmon, *First Comes the Baby Carriage*, N.Y. Times Oct. 13, 2005, at G.1 (“You’re paying for it, so you kind of want the best of the best.”).

²²³ This incentive was acknowledged by the *Johnson* Court. See *Johnson v. Superior Court (Johnson II)*, 124 Cal. Rptr. 2d 650, 660 (Cal. Ct. App. 2002) (“A wide variety of factors leads individuals to their decision to use [AI] including genetic disorders.”); Helen M. Alvare, *The Case for Regulating Collaborative Reproduction: A Children’s Rights Perspective*, 40 Harv. J. on Legis. 1, 25 (2003) (arguing that “[t]he industry is in the business of selling superior genetic

quality that many of them seek by not affording them appropriate legal remedies when they and their DRT children are injured defeats one of the main reasons for using DRT.

From a torts policy point of view, the current regulatory scheme is contrary to notions of justice and economic efficiency.²²⁴ As explained above, DRT recipients are the least informed and least equipped party to assess the genetic risks involved in the use of DRT. Moreover, under the current regulatory scheme, DRT recipients run the most significant risk involved in the use of DRT—giving birth to very sick individuals. Meanwhile, DRT institutions that could have prevented the injury most efficiently and effectively, and which are also the “deep pocket,” are left practically unscathed.²²⁵ This situation is not only inefficient from an economic standpoint but also offensive from distributive and corrective justice points of view.

It is prudent to assume that with the persistently high number of individuals using DRT, constant improvement in preconception diagnosis technology and the maturation of DRT children (and manifestation of dormant genetic diseases), claims of DRT children and recipients, which are still relatively rare, will increase in number.²²⁶ In other words, unless the regulatory framework is changed, the problems stemming from the current regulatory scheme are only going to be aggravated.

In sum, the DRT market, given its particular characteristics, is currently under-regulated to an extent that poses a significant risk to the lives, health and welfare of a large and ever growing population of DRT recipients and DRT children.²²⁷ In the several decades since ART became available to the public, the federal government, states, courts and professional organization have all failed to create a coherent regulatory scheme that would protect DRT recipients, DRT children and the public from avoidable genetic hazards involved in DRT.²²⁸ This type of systemic failure calls for the involvement of

inheritances for high fees”); Ginsberg, *supra* note 96, at 823, 827-28 (“[M]any recipients use artificial insemination to avoid passing a genetic disease to their children.”); Peterson, *supra* note 69, at 62-63 (asserting that the second most common reason for the use of AI is that the intended father carries a genetic mutation which the intended parents fear transmitting to their child).

²²⁴ See Hodgson, *supra* note 96, at 359 (calling for increased moral accountability and legal liability where economizing the results of the creation of “low-cost, low-quality human offspring”).

²²⁵ Indeed, the settlement amounts of over \$1M in the *Johnson* and *Paretta* cases are significant. Yet, they did not include any punitive component and, arguably, were not substantial enough to create a deterrent effect.

²²⁶ See Browne, *supra* note 96, at 2591. See also Denise Grady, *As the Use of Donor Sperm Increases, Secrecy Can Be a Health Hazard*, N.Y. Times, June 6, 2006, at F5, available at <http://www.nytimes.com/2006/06/06/health/06opin.html>.

²²⁷ See Parens & Knowles, *supra* note 201, at S12, S14 (arguing that although many groups and federal agencies have commented on or asserted authority over DRT, “there is, at best, a patchwork system of oversight” which calls for improved government oversight)

²²⁸ Notably, numerous commentators have highlighted the lack of protection of DRT children as especially problematic. See generally Alvare, *supra* note 223, at 25-26 (arguing that the DRT industry accommodates and prefers the interests of adults over the needs and well-being of

the federal government.²²⁹ As discussed *infra* in Part IV, the FDA is the federal government branch best positioned for and capable of regulating the genetic aspects of DRT and has the authority to do so. By way of comparison, the next section describes the federal-like regulation of genetic aspects of DRT in the European Union and exemplifies some of its features that may be “imported” to a similar future scheme in the United States.

III. THE REGULATION OF GENETIC ASPECTS OF DONATED REPRODUCTIVE TISSUE IN EUROPE

Given its unique history and circumstances, regulation in the United States generally, and that of reproductive technologies in particular, is not comparable to the regulation in other countries. However, there is merit in observing how some of the problems that plague the regulation of this area in the United States are addressed in Europe so that similar solutions may be crafted for the regulation of DRT in the United States.

A. The European Union

Article 152(4)(a) of the Treaty Establishing the European Community gives the European Union (“E.U.”) the mandate to pass laws on the quality and safety of human tissues and cells.²³⁰ In light of the fact that many DRT recipients acquire their DRT through cross-border exchange, the E.U. sought to create uniformity of standards among member states so that E.U. citizens would benefit from the same protection as they would under the laws of their own country.²³¹ Accordingly, in 2004, the E.U. issued the Tissues and Cells Directive, which established rules and principles meant to ensure the safety and quality of DRT in E.U. countries.²³² The 2004 Directive recognized that

children); Rosato, *supra* note 201, at 62, 69 (noting that “[t]he market rules and no one in the entire contracting process speaks for the future child” and “it does not appear that self-regulation sufficiently protects children and is unlikely to do so in the near future”). Some commentators reached the same conclusion over a decade ago. See Ginsberg, *supra* note 96, at 823-41 (arguing that state-by-state regulation, self-imposed guidelines and private adjudication have all proven inadequate for regulating the artificial insemination industry and calling for federal regulation of the screening and testing of donated sperm).

²²⁹ See Annas, *supra* note 22, at 938 (concluding that “it will probably take federal action to move children to the center of consideration in the fertility business”).

²³⁰ Consolidated Versions of the Treaty on European Union and of the Treaty Establishing the European Community art. 152, Dec. 29, 2006, 2006 O.J. (C321) 115, available at <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2006:321E:0001:0331:EN:pdf>.

²³¹ See Press Release, Europa, Questions and Answers on Human Tissues and Cells (Feb. 8, 2006), available at <http://europa.eu/rapid/pressReleasesAction.do?reference=MEMO/06/66>.

²³² See Council Directive 2004/23, 2004 O.J. (L102) 48-58 (EC) [hereinafter 2004 Directive].

[t]he use of tissues and cells for application in the human body can cause diseases and unwanted effects . . . [most of which] can be prevented by careful donor evaluation and the testing of each donation in accordance with rules established and updated according to the best available scientific advice.²³³

Accordingly, the 2004 Directive required each member state to establish a system for the accreditation of tissue establishments and for notification regarding adverse events linked to the testing and distribution of tissue.²³⁴ The 2004 Directive further required setting donor selection criteria and donor testing requirements and stipulated that member states were required to pass appropriate laws and regulations to implement the 2004 Directive no later than April 7, 2006.²³⁵

Subsequently, in 2006, the European Commission issued two additional directives expanding on the 2004 Directive. The first directive, 2006/17, covered the collection and processing of reproductive tissue.²³⁶ Recognizing that “[r]eproductive cells have, due to the specific nature of their application, specific quality and safety characteristics,”²³⁷ 2006/17 requires that the use of reproductive cells other than for directed donation must meet several criteria, including:²³⁸ (1) donors must be selected on the basis of their age, health and medical history, as determined based on a questionnaire and a personal interview performed by healthcare professionals;²³⁹ (2) a decision to use any particular DRT must be based on an assessment of the risk of transmission of inherited conditions known to be present in the donor’s family and genetic testing for autosomal recessive genes known to be prevalent in the donor’s ethnic background; and (3) the recipient must receive a clear explanation of all of the information about the risks associated with using the DRT and the measures undertaken to mitigate them.

Later in 2006, the European Commission issued another directive, 2006/86, that imposed several additional requirements related to the processing of DRT and to the traceability and reporting of serious adverse events.²⁴⁰ 2006/86 requires tissue manufacturers to have procedures in place to retain records of tissues and cells they

²³³ *Id.* at Whereas 17.

²³⁴ *Id.* at Whereas 25; arts. 11, 15.

²³⁵ *Id.* at arts. 28, 31.

²³⁶ *See* Council Directive 2006/17 2006 O.J. (L38) 40-52 (EC) [hereinafter 2006/17].

²³⁷ *Id.* at Whereas 4.

²³⁸ *Id.* at Annex III § 3.

²³⁹ Specifically, the 2006 Directive requires that different sources of information be used to obtain the relevant information, including an interview with the donor (mandatory), review of the donor’s medical records and their evaluation by a qualified health professional, interview with the donor’s treating physician and physical examination of the donor. *Id.* at Annex IV § 1.2.

²⁴⁰ *See* Council Directive 2006/86 2006 O.J. (L204) 23-36 (EC) [hereinafter 2006/86].

procured and to immediately report to the appropriate authorities and other tissue establishments serious adverse conditions in a donor that may reflect on the quality and safety of a donated tissue.²⁴¹ The Directive further stipulates that the records must be kept for a period of at least thirty years and that all data be coded in a unified single European identification code system.²⁴²

In conclusion, the E.U. adopted a mandatory framework requiring, among other things, the genetic screening and testing of DRT donors and reporting adverse events, including those suspected as having a genetic background. I will now discuss implementation of the 2004 and 2006 Directives (E.U. Directives) in the United Kingdom and Ireland.

B. The United Kingdom

Even before the European Commission issued the E.U. Directives, matters involving DRT were regulated in the United Kingdom under the Human Fertilisation and Embryology Act (HFE Act).²⁴³ On May 25, 2007, a new set of regulations went into effect that extensively amended and supplemented the HFE Act to comply with the E.U. Directives.²⁴⁴ The HFE Regulations included a list of requirements pertaining to the procurement and distribution of DRT, operation of a DRT institution and engaging in various related activities. In particular, the HFE Regulations required DRT institutions to keep records containing information regarding the quality and safety of gametes and embryos and any information necessary to trace gametes and embryos back to their donors.²⁴⁵ The HFE Regulations further required that the British Human Fertilisation and Embryology Authority (HFEA) investigate serious adverse events related to DRT and fertilization and communicate to the European Commission and parallel authorities in other member states relevant information which may assist in withdrawal of compromised DRT.²⁴⁶

Most importantly, with respect to donations of gametes or embryos other than between partners, the HFE Regulations stipulate that DRT institutions must comply with the selection criteria for donors and the requirements for laboratory tests set forth in Section 3 of Annex III of 2006/17.²⁴⁷ Specifically, the HFE Regulations require the

²⁴¹ *Id.* at art. 5, Annex VI.

²⁴² *Id.* at arts. 9-10.

²⁴³ Human Fertilisation and Embryology Act, 1990, c. 37 (Eng.).

²⁴⁴ Human Fertilisation and Embryology (Quality and Safety) Regulations, 2007, S.I. 2007/1522 (U.K.) [hereinafter HFE Regulations].

²⁴⁵ *Id.* at § 13.

²⁴⁶ *Id.* at §§ 10, 18.

²⁴⁷ *Id.* at § 30, Annex 3A § 7.

selection of donors on the basis of their age, health and medical history and an assessment of the risk of transmission of inherited conditions known to be present in the donor's family as well as genetic testing for autosomal recessive genes known to be prevalent in the donor's ethnic background.²⁴⁸ In other words, in order to receive a license under the HFE Act, a DRT institution must have in place an appropriate framework for the minimization of the genetic risks to DRT children.

In addition, the HFEA has published a Code of Practice that expands upon and clarifies the requirements set forth in the amendments to the HFE Act.²⁴⁹ According to the HFEA Code, DRT institutions must not collect sperm from donors older than forty-six or harvest ova from donors older than thirty-six²⁵⁰ and should not use DRT from any specific donor in more than ten families.²⁵¹ The HFEA Code requires DRT institutions to take donors' family medical histories and test donors as necessary based on the risk factors identified.²⁵² The HFEA Code further directs DRT institutions to follow contemporary professional guidance of relevant professional bodies on the genetic tests and screening techniques they should implement.²⁵³ In particular, the HFEA Code mentions the guidelines of the British Andrology Society and the British Fertility Society.²⁵⁴

²⁴⁸ See *supra* note 238 and accompanying text. Notably, an additional requirement is that the recipient must receive a clear explanation of complete information on the genetic risks associated with the gametes received and on the measures undertaken for their mitigation.

²⁴⁹ The Human Fertilisation and Embryology Authority, Code of Practice (7th ed. 2008) [hereinafter *HFEA Code*], available at http://www.hfea.gov.uk/docs/Seventh_Edition__R3.pdf.

²⁵⁰ *Id.* at §§ G.4.2.1-G.4.2.2.

²⁵¹ *Id.* at § G.4.6.1.

²⁵² *Id.* at §§ G.4.7.1-G.4.7.2.

²⁵³ *Id.* at § G.4.9.1.

²⁵⁴ *Id.* See also Ass'n of Biomedical Andrologists et al., UK Guidelines for the Medical and Laboratory Screening of Sperm, Egg and Embryo Donors, 11 Human Fertility 201, 201 (2008) [hereinafter *British Professional Guidelines*]. The British Professional Guidelines set forth an extensive list of tests that DRT institutions and practitioners should perform and instructions to be followed as part of the donor screening and selection procedures. Importantly, the British Professional Guidelines stipulate that when taking medical histories of potential donors, inquiries should be made to ensure that the donor does not have "familial disease with a major genetic component . . . any significant Mendelian disorders, such as (but not exclusively) albinism, hemophilia, hemoglobin disorders," "familial disease with a known or reliably indicated major genetic component, such as debilitating asthma, juvenile diabetes mellitus, epileptic disorder," "a chromosomal rearrangement that may result in unbalanced gametes," and more. *Id.* at 203. The British Professional Guidelines further instruct that "the potential donor should ordinarily not be heterozygous for an autosomal recessive gene for a disease known to be prevalent in the donor's ethnic background, e.g., CF in Caucasian populations, α^0 or β -Thalassemia in Mediterranean populations, sickle cell disease in African & Afro-Caribbean populations and Tay-Sachs disease

Finally, the HFEA Code imposes duties on DRT institutions to notify the appropriate authorities, other institutions *and recipients* once they discover “that a gamete donor has a previously unsuspected genetic disease or is the carrier of a deleterious recessively inherited condition.”²⁵⁵

C. Ireland

As a member state in the European Union, Ireland was also required to incorporate the E.U. Directives into its legislation and did so with two sets of regulations promulgated by the Irish Minister for Health and Children and administered by the Irish Medicine’s Board (IMB).²⁵⁶ Under S.I. No. 158, in order to be licensed to engage in the collection and distribution of DRT, institutions must comply with numerous donor selection and testing requirements.²⁵⁷ S.I. No. 158 stipulates that donors must be selected on the basis of their age, health and medical history, which the donor should provide on a questionnaire and in a personal interview by a healthcare professional.²⁵⁸ S.I. No. 158 further requires the “[g]enetic [test]ing for autosomal recessive genes known to be prevalent . . . in the donor’s ethnic background and an assessment of the risk of transmission of inherited conditions known to be present in the family” and stipulates that “[c]omplete information on the associated risk and on the measure undertaken for its

in Jews of Eastern European descent. The British Professional Guidelines also dictate that inquiries should be made to verify that the potential donor’s genetic parents, siblings and offspring are free of (1) major malformations listed in the British Professional Guidelines, (2) non-trivial disorders showing Mendelian inheritance e.g., autosomal dominant disorders, such as Huntington’s disease and autosomal recessive diseases, particularly if such diseases have a high frequency in the population such as CF, (3) a chromosomal abnormality (unless the donor has a normal karyotype) and (4) in egg and embryo donors, a history of any mitochondrial disorders. If there is any evidence of any of the above, the British Professional Guidelines instruct that a qualified clinical geneticist should evaluate the risk. *Id.* The British Professional Guidelines also require that “[a]ll donors should undergo appropriate genetic/cytogenetic testing” which includes karyotyping of all donors, and testing according to ethnic background for α^0 or β -Thalassemia, sickle-cell disease, Tay-Sachs disease and common mutations of CF. *Id.* at 204.

²⁵⁵ *HFEA Code*, *supra* note 249, at § G.4.10.5.

²⁵⁶ *See* European Communities (Quality and Safety of Human Tissues and Cells) Regulations 2006 (S.I. No. 158 of 2006) (Ir.) [hereinafter S.I. No. 158], *available at* <http://www.irishstatutebook.ie/2006/en/si/0158.html> (implementing 2004/23 and 2006/17); European Communities (Human Tissues and Cells Traceability Requirements, Notification of Serious Adverse Reactions and Events and Certain Technical Requirements) Regulations 2007 (S.I. No. 598 of 2007) (Ir.) [hereinafter S.I. No. 598] *available at* <http://www.irishstatutebook.ie/2007/en/si/0598.html> (implementing 2006/86).

²⁵⁷ S.I. No. 158 at §§ 5-6, 11(2), 11(6).

²⁵⁸ *Id.* at Schedule 3, § 3.1.

mitigation must be communicated and clearly explained to the recipient.”²⁵⁹ S.I. No. 598 supplements the regulatory framework created in S.I. No. 158 by imposing traceability and adverse events reporting requirements as directed by 2006/86.²⁶⁰

The European model of regulation of the genetic aspects of DRT could be characterized as relying on three premises. First and foremost, the recognition that “while those seeking assisted reproductive treatment deserve and can expect proper consideration of their medical and social needs, licensed treatments may result in children who would not otherwise have been born and whose interest must be taken into account.”²⁶¹ Second, the structure of the European regulations reflects the recognition that the protection of DRT children (and their families) requires the uniformity and authoritativeness that can only be afforded by legislation and regulation. And third, the European regulatory framework, while setting general principles and requirements, leaves the actual “nuts and bolts” to be decided by professionals who have the necessary technical knowledge and expertise; in this respect, state authorities serve as a facilitator and enforcer of professional standards.

An additional advantage of the European model of regulation is that it enables state authorities to defer possible bioethical issues to professionals who, by virtue of their expertise and involvement in the regulated area, are best equipped to tackle such issues.²⁶² The “importation” of professional standards into the regulatory framework enables state authorities to avoid having to spend the time and money necessary for tackling bioethical issues as well as possible political strife (which administrative entities are loathe to provoke) involved with delving into bioethical debates.²⁶³

Despite the particularities of the United States legal system, the three abovementioned premises of the European regulation of genetic aspects of DRT can be adapted into a feasible model for federal regulation in the United States’ in a fashion that would resolve many of the problems that characterize the current regulation of genetic aspects of DRT.

IV. TOWARDS FEDERAL REGULATION OF THE GENETIC ASPECTS OF DONATED REPRODUCTIVE TISSUE—THE CASE FOR FDA REGULATION

The first and most important advantage of federal regulation of genetic aspects of DRT would be the institution of a uniform and feasibly enforceable standard of conduct that would increase adherence of DRT institutions to testing standards thereby promoting safety for DRT children regardless of the origin of the DRT from which they were

²⁵⁹ *Id.* at Schedule 3, § 3.6.

²⁶⁰ *See* S.I. No. 598 at §§ 5-22.

²⁶¹ *HFEA Code*, *supra* note 249, at § 1.2.

²⁶² For further discussion, see *infra* Part IV.B.4.

²⁶³ Notably, this approach may be especially fitting to the United States, where disagreements on bioethical issues often run deep.

conceived.²⁶⁴ In other words, the main function of federal regulation of the genetic aspects of DRT would lie in its general applicability. Assuming that most DRT institutions and practitioners would do their best to conform to such standards, the safety of using DRT from a genetic standpoint could increase dramatically.²⁶⁵

Second, the high enforceability of federal regulations²⁶⁶ and adherence to them would serve to preempt many occurrences of transmission of genetic diseases to DRT children in the first place, thereby providing an *ex ante* solution to avoid cases like *Johnson and Paretta*.

Third, the imposition of a federal standard of conduct would diminish the need for injured DRT children and their families to resort to *ex post* solutions. Third, the imposition of a federal standard of conduct would, at the very least, strengthen the legal stances of DRT children and their families. A standard set by federal regulations may be accepted by courts as the standard of conduct by which the actions of DRT professionals should be evaluated when a negligence claim is brought, thereby enabling a quick and efficient resolution of such matters.²⁶⁷ Federal standards of conduct set by federal

²⁶⁴ See Annas, *supra* note 22, at 938 (“it will probably take federal action to move children to the center of consideration in the infertility business”); *Human Tissues and Organs*, *supra* note 104, at 46-47, 56 (“Unfortunately for those of us in the semen banking business we don’t necessarily know which states have [put regulations in place]. . . I would highly support the FDA in regulating semen banking,” “FDA standard seems far more likely to prevent state variances than voluntary standards.”).

²⁶⁵ *Human Tissues and Organs*, *supra* note 104, at 56 (“[A]nother advantage of government standards is their ability to reassure the public . . . FDA’s involvement would moot [the] concern [that voluntary standards and adherence to them are lacking.]”). Federal regulation of genetic aspects of DRT would also serve to assure consumers in every state and U.S. territory that the DRT they acquire is indeed safe without them having to become experts in clinical genetics.

The need for a generally applicable regulation of the genetic aspects of DRT is further highlighted by the lack of such applicability of state regulation. Since many DRT recipients order their DRT from states other than those in which they live, even the few states that do seek to regulate the genetic aspects of DRT are likely to find the enforcement of such regulation difficult, if not impossible. It would be impractical and unrealistic to expect that New York State, for example, would verify that every semen specimen sent *via* overnight delivery to consumers within its borders was processed, screened and tested in accordance with the New York Regulations.

²⁶⁶ It is preferable that—like the Human Tissue Regulations—federal regulations pertaining to the genetic aspects of DRT be enforced by the FDA.

²⁶⁷ Since the Human Tissue Regulations only address the communicable diseases aspects of DRT, DRT institutions sued for negligence in their genetic screening and testing of DRT donors could raise a regulatory compliance defense arguing that they are in full compliance with the federal standard of practice with respect to the genetic screening and testing of DRT and therefore cannot be held liable for incompliance with higher standards set by the states. Similarly, DRT institutions could raise federal preemption arguments seeking to preempt such heightened state standards in view of the non-existent federal standard of practice with respect to the genetic aspects of DRT. For a discussion of regulatory compliance and federal preemption defenses, see

regulations could also serve to preempt outright refusal by courts to recognize the existence of additional causes of action available to DRT recipients, as was done by the *Paretta* court.²⁶⁸ Finally, the imposition of duties as part of federal regulation may potentially provide plaintiffs with additional causes of action for breach of statutory duty, which may further assist in securing appropriate relief for genetically injured DRT children and their families.²⁶⁹

The FDA is the natural and most promising candidate for carrying out and enforcing federal regulation of the genetic aspects of DRT. As discussed above, the FDA has been involved in regulation of donated tissues since the late 1990s and DRT since 2001. It is prudent to assume that the FDA has acquired much of the technical expertise and understanding of the DRT market necessary to also regulate the genetic aspects of DRT in an effective and efficient manner. Thus, it would be desirable to utilize the FDA's acquired expertise as well as its proven abilities in enforcing the Human Tissue Regulations²⁷⁰ in the regulation of the genetic aspects of DRT.²⁷¹

The idea of having the federal government, and specifically the FDA, regulate the genetic aspects of DRT is not a new one and has been raised time and again, at least since 1988.²⁷² And yet, in promulgating its relatively recent Human Tissue Regulations, the

Wyeth v. Levine, 129 S.Ct. 1187, 1194-95 (2009); Carl Tobias, *FDA Regulatory Compliance Reconsidered*, 93 Cornell L. Rev. 1003, 1004 (2008). A discussion of federal preemption is beyond the scope of this Article. A comprehensive federal regulatory standard of practice could prevent DRT institutions from avoiding liability by raising these defenses. *See also supra* note 101 and accompanying text.

²⁶⁸ *See supra* notes 134 and 136 and accompanying text.

²⁶⁹ For additional possible advantages of setting uniform regulatory standards for DRT see *Human Tissue and Organs*, *supra* note 104, at 53-54.

²⁷⁰ *See, e.g.*, HTTF Report, *supra* note 67 (discussing the FDA's enforcement of the Human Tissue Regulations).

²⁷¹ In this respect, due to the rapidly changing and technically complicated nature of the area of genetic medicine and ART, the FDA would also be better suited than Congress to address issues as they arise. *See Alvarez*, *supra* note 223, at 32 ("The size and scope of the legislative project—even the definition of individual and the social dilemmas to be approached—may appear too large and too rapidly changing a target for legislatures."). The regulation of genetic aspects of DRT may coincide with the FDA's own perception of its mission with relation to the regulation of human tissue. *See Zoon Statement*, *supra* note 59, at 88-89, 101 ("FDA has prioritized the regulation of human cellular and tissue-based products, and the public should be confident that the FDA is committed to regulating these products in a manner where benefits to patients are maximized and risks to patients are minimized;" "FDA's goals are to protect the public from unsafe tissue products.").

²⁷² *See GAO 1997 Report*, *supra* note 182, at 3-4, 31 ("FDA should also add to its oversight plans provisions that would require . . . disclosure of genetic tests that have been performed on donated reproductive tissues."); Annas, *supra* note 22, at 935; Marwick, *supra* note 27, at 1340 (describing [then] Senator Gore's call for FDA regulation of DRT, including its genetic aspects, to ensure the safety and welfare of DRT children).

FDA sought only to regulate the communicable diseases aspects of DRT.²⁷³ Notably, the FDA did not address the genetic aspects of DRT at any point in the process of promulgating the Human Tissue Regulations and the issue never arose in any of the abundant public commentary on the proposed FDA regulations.²⁷⁴

It is highly unlikely that the FDA was unaware of the genetic aspects of DRT in 2005 when it issued the Final Donor Eligibility Rule.²⁷⁵ In fact, at the time it promulgated the Final Donor Eligibility Rule, the FDA was aware of professional guidelines that specifically addressed the genetic aspects of DRT²⁷⁶ and probably had knowledge of good reasons for regulating the genetic aspects of DRT.²⁷⁷ It therefore appears that the absence of genetic aspects of DRT from the Human Tissue Regulations was not the result of an oversight but rather intentional avoidance of this area by the FDA.

²⁷³ See *supra* note 60 and accompanying text.

²⁷⁴ It is likely that since, from the outset, the FDA defined the Human Tissue Regulations as directed exclusively to the communicable diseases aspects of DRT, it chose not to make public any comments it may have received that were related to the genetic aspects of DRT as, purportedly, irrelevant to the Human Tissue Regulations. It is also possible that the FDA has made it so abundantly clear that the Human Tissue Regulations, by definition, were only meant to address communicable diseases aspects of human tissue, that commentators refrained from addressing the genetic aspects of DRT. See *infra* Part IV.A.

²⁷⁵ See *supra* notes 47-60 and accompanying text.

²⁷⁶ For example, in 2004, the ASRM issued an updated version of its Guidelines, which the FDA referred to during the process of making the FDA Final Donor Eligibility Rule. See 69 Fed. Reg. 29819 (FDA May 25, 2004) (“Although ASRM has published guidelines for donor screening and testing and other aspects of oocyte donation . . .”).

²⁷⁷ Among the rationales for regulation mentioned in the FDA Final Donor Eligibility Rule was concern for public health that is equally applicable to genetic and communicable diseases aspects of DRT:

Certain diseases are transmissible through the implantation, transplantation, infusion or transfer of [donated tissue] . . . To prevent the introduction, transmission, or spread of such diseases, we consider it necessary to take appropriate measures to prevent the use of cells or tissue from infected donors. Thus, these regulations require that, before the use of most [donated tissues], the cell or tissue donor must be determined to be eligible to donate, based on the results of screening and testing for relevant . . . diseases. In most cases, a donor who . . . possesses clinical evidence of or risk factors for such a disease, would be considered ineligible, and cells and tissues from that donor would not ordinarily be used.

See *FDA Final Donor Eligibility Rule*, *supra* note 24, at 29787.

A. The FDA's Statutory Authority to Regulate the Genetic Aspects of Donated Reproductive Tissue

There are several possible explanations for the FDA's failure to regulate the genetic aspects of DRT, the first of which is possible doubts regarding its legal authority to do so. As mentioned earlier, in promulgating the Human Tissue Regulations, the FDA relied on PHSA § 361, which reads, in relevant part, as follows:²⁷⁸

Regulations to control communicable diseases

(a) Promulgation and enforcement by Surgeon General^[279]

The Surgeon General . . . is authorized to make and enforce such regulations as in his judgment are necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the States or possessions, or from one State or possession into any other State or possession. For purposes of carrying out and enforcing such regulations, the Surgeon General may provide for such inspection . . . destruction of animals or articles found to be so infected or contaminated as to be sources of dangerous infection to human beings, and other measures, as in his judgment may be necessary.

Arguably, PHSA § 361 grants only the authority to promulgate regulations pertaining to the prevention of the transmission and spread of infectious diseases rather than genetic diseases.²⁸⁰ Under this construction of “communicable diseases,” PHSA §

²⁷⁸ PHSA § 361 (codified at 42 U.S.C. § 264).

²⁷⁹ As mentioned earlier, the authority under PHSA § 361 was delegated to the FDA. *See supra* note 62.

²⁸⁰ This reading of PHSA § 361 relies on a construction of the definition of “communicable diseases” as only reasonably including diseases caused by infectious agents rather than by chromosomes and genes. The term “communicable diseases” is not defined in the PHSA. However, 21 C.F.R. § 1240.3(b) defines “communicable diseases” as “[i]llnesses due to infectious agents or their toxic products, which may be transmitted from a reservoir to a susceptible host either directly as from an infected person or animal or indirectly through the agency of an intermediate plant or animal host, vector, or the inanimate environment.” Notably, this restrictive definition was created pursuant to the legislation of PHSA § 361 and is in accord with its legislative history, which only sought to address infectious diseases as these are defined by the FDA. Yet, under a liberal view on the duties and authorities of executive agencies, should the FDA ever choose to change its definition of “communicable diseases” to include genetic diseases, it may, arguably, be able to do so, subject the requirements of the Administrative Procedure Act. *See* 5 U.S.C. §§ 551(5), 553. Moreover, it is not clear how scientifically sound the 42 U.S.C. § 361 dichotomy between communicable and genetic diseases is and whether it is justifiable from a public health policy perspective. For example, many diseases could be branded as both infectious and genetic (e.g., HIV, cervical cancer caused by a viral infection). Nonetheless, for purposes of the discussion herein, the term “communicable diseases” is

361 could not serve as a source of authority to regulate genetic aspects of DRT. Such authority, however, exists elsewhere.

Among the several other possible routes for regulation of genetic aspects of DRT suggested in the past,²⁸¹ the most promising source of authority is PHSA § 351,²⁸² which reads, in relevant part, as follows:²⁸³

Regulation of biological products

(a) Biologics license

(1) **No person shall introduce or deliver for introduction into interstate commerce any biological product unless—**

(A) **a biologics license is in effect for the biological product**

(2) (A) The Secretary shall establish, by regulation, requirements for the approval, suspension, and revocation of biologics licenses.

(C) The Secretary shall approve a biologics license application—

(i) on the basis of a demonstration that—

(I) **the biological product that is the subject of the application is safe, pure, and potent; and**

(3) The Secretary shall prescribe **requirements under which a biological product undergoing investigation shall be exempt from the requirements of paragraph (1).**

(i) Definition; application

In this section, the term “biological product” means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or **analogous product** . . . applicable to the **prevention, treatment, or cure of a disease or condition of human beings.**

(emphasis added)

construed as exclusive of diseases having genetic background (but not diseases resulting from viral infections).

²⁸¹ See, e.g., Hodgson, *supra* note 96, at 360-85 (advocating treating the sale of sperm as a “sale” rather than as a “service” under the U.C.C.); Parens & Knowles, *supra* note 201, at S19 (calling for the creation of an HFEA-like body in the United States which would license institutions participating in ART related activities).

²⁸² See *Human Tissue and Organs*, *supra* note 104, at 14, 19, 21-22; Peterson, *supra* note 69, at 88.

²⁸³ PHSA § 351 (codified at 42 U.S.C. § 262 (2007)).

The FDA construes the PHSA § 351(i) definition of “biological product” as follows:²⁸⁴

Biological products include a wide range of products such as . . . somatic cells . . . [and] tissues. . . . Biologics . . . may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources - human, animal, or microorganism

Thus, according to the FDA, “biological products” include human cells and tissues.²⁸⁵ PHSA § 351(i) also clarifies that biological products do not necessarily have to be used as cures for diseases but could serve *for the treatment of a condition of a human being*. Arguably, even if infertility cannot be categorized as a disease in the conventional sense,²⁸⁶ it could still fall within the boundaries of a “condition of a human being” which could be “prevented” or “treated” *via* the use of DRT.²⁸⁷ Thus, the PHSA § 351(i) definition of “biological product” could conceivably encompass DRT such that PHSA § 351 would give the FDA authority to regulate DRT as a biological product.²⁸⁸

Admittedly, it is possible to imagine several scenarios where the use of DRT does not fall within the PHSA § 351(i) definition of biologics. For example, it is difficult to classify as “treatment” the use of donated sperm to impregnate a perfectly fertile woman whose husband suffers from infertility.²⁸⁹ Similarly, it is difficult to classify as

²⁸⁴ See FDA, What Are “Biologics” Questions and Answers, <http://www.fda.gov/AboutFDA/CentersOffices/CBER/ucm133077.htm> (last visited May 10, 2010).

²⁸⁵ Although the FDA’s definition only specifically mentions somatic cells, it does not exclude reproductive cells and the denominator “such as” indicates that somatic cells are only mentioned as an example. Thus, it appears that reproductive cells could also be biological products under the FDA definition.

²⁸⁶ See Andrews & Elster, *supra* note 70, at 37.

²⁸⁷ See Peterson, *supra* note 69, at 88 (“[T]he phrase ‘analogous product’ easily could be interpreted to include semen samples The straws containing the frozen semen derivative could easily be categorized as a ‘biological product’ which is applicable to the ‘treatment or cure’ of human infertility diseases.”).

²⁸⁸ Interestingly, this also appears to have been the opinion of the FDA’s General Counsel in 1973. See *Human Tissues and Organs*, *supra* note 104, at 5 (presentation of Stuart Nightingale, Associate Comm’r for Health Affairs, FDA); Merrill, *supra* note 23, at 9 (presenting the response of the Chief Counsel: “Human tissues . . . could be considered ‘analogous’ to materials such as blood, over which FDA had authority under section 351”). Similar positions were presented by Paul Parkman, the Director of CBER in 2001. See *Human Tissues and Organs*, *supra* note 104, at 22.

²⁸⁹ The reason for this is that the person who is actually being “treated” (i.e., the female) is not the one actually suffering from infertility.

“treatment” the use of DRT due to a couple’s wish to avoid passing along a genetic condition existing in one of them.²⁹⁰ Even more significantly, it would be difficult and even disturbing to classify the use of sperm by single women or of DRT by single-sex couples as a “cure” or “treatment.” Yet, there are obviously many situations in which the use of DRT would fall neatly within the boundaries of PHSA § 351(i) and which ought to be “sufficient,” from a regulatory perspective, to deem DRT suitable for regulation under PHSA § 351.²⁹¹

Furthermore, broad construction of the term “condition of human beings” could conceivably encompass almost any scenario involving the use of DRT and it does not have to be construed as relating to a medical condition but rather as relating to a social or familial situation or even status, e.g., infertility (as a couple or family), childlessness or the inability to have children on one’s own or with one’s chosen partner. In view of the above, it is highly unlikely that courts would reject a construction of PHSA § 351(i) that would encompass reproductive tissue within the definition of biological products thereby facilitating the application of this section to DRT.²⁹²

²⁹⁰ The reason is that it is not the genetic condition that is being treated. Rather, the underlying reason for using DRT is the couple’s reproductive preferences.

²⁹¹ Examples of scenarios that fit into the PHSA § 351(i) framework would include the use of donated eggs to enable women who no longer ovulate to conceive, in which case the donated eggs could be perceived as “treatment” for such women’s “condition” of infertility; using donated sperm in tandem with IVF treatments, in which case the donated sperm is the “treatment” for the husband’s inability to provide sperm to fertilize the eggs in order to create embryos that would be implanted into his female partner or into a surrogate.

²⁹² It is well accepted that agencies have discretion to interpret their statutory authorities to enable their application in new ways to meet new challenges unforeseen by Congress and that they are *expected* to do so. *See infra* note 297 and accompanying text. Accordingly, although Congress might not have envisioned the use of PHSA § 351 for regulating DRT when it enacted the section, it is well within the power of the FDA to apply this section to such an end so long as its construction of the statutory language meets the *Chevron* standard. *See Chevron U.S.A. Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 842-44 (1984) (“We have long recognized that considerable weight should be accorded to an executive department’s construction of a statutory scheme . . .”). Under what came to be called the “*Chevron* Doctrine,” courts generally grant agencies’ discretionary decisions and actions a great measure of deference and are not easily persuaded to set them aside so long as (1) “Congress has [not] directly spoken to the precise question at issue,” and (2) “the agency’s answer is based on a permissible construction of the statute.” *See id.* at 842-44. According to the Supreme Court, if both conditions are met, then the agency’s construction of the statute it is entrusted to administer should receive “considerable weight” and “the principle of deference to administrative interpretations [should be] followed.” *Id.* Given the plausibility of viewing DRT as biological products under at least some circumstances that fall neatly within the boundaries of PHSA § 351(i) and the fact that PHSA § 351 does not address reproductive tissue in general or DRT in particular, it is likely that courts would accept an agency’s construction of PHSA § 351(i) as inclusive of DRT. Notably, this entire regulatory conundrum could be resolved if Congress were to amend PHSA § 351(i) so it explicitly included reproductive tissue, thereby also indicating that DRT should be comprehensively regulated by the FDA.

Despite possible concerns that if DRT were to be regulated as a biological product every sperm sample would require its own separate approval and licensure, PHSA § 351(a)(3) provides the FDA with the authority to exempt a biological product from the licensure requirements of PHSA § 351(a)(1). Thus, when promulgating a regulatory framework that would address genetic aspects of DRT, the FDA could conceivably stipulate, for example, that DRT coming from a donor who was properly screened and tested in accordance with regulations promulgated under PHSA § 351(a)(2) would be exempt (under PHSA § 351(a)(3)) from the burdensome licensure requirements of PHSA § 351(a)(1).

PHSA § 351 also provides the FDA with effective enforcement tools that include (1) the authority to inspect DRT institutions engaging in collection, processing or distribution of DRT²⁹³ and (2) the authority to determine whether DRT originating from a specific donor would present an imminent or substantial hazard to public health and to issue orders for the recall of such DRT.²⁹⁴ Furthermore, in addition to any deterrents and incentives the FDA may include in regulations promulgated under PHSA § 351 to ensure effective enforcement of the regulation of biologics, violation of PHSA § 351 is a criminal offense, punishable by fines and up to one year in prison; it also sets a civil penalty of up to \$100,000 per day for non-compliance with an order recalling a biological product.²⁹⁵ Thus, PHSA endows the FDA with ample authority and sufficient enforcement tools to effectively regulate the genetic aspects of DRT.

B. Other Possible Reasons for the FDA's Non-Regulation of Genetic Aspects of Donated Reproductive Tissue

1. Lack of Authority to Tend to the Safety of Future People

Under a narrow construction of the FDA's authority under PHSA § 351, the FDA's power is arguably limited only to the assurance of the safety of DRT recipients rather than that of DRT children.²⁹⁶ Such a reading of FDA authority appears to be unnecessarily and unjustifiably narrow, especially in light of the conventional understanding that agencies have discretion and are expected to interpret their statutory authority so it applies in new ways to meet new challenges that Congress did not

²⁹³ 42 U.S.C. § 262(c) (2007) (granting the FDA authority to inspect any establishments engaging in the propagation or manufacture and preparation of any biological product).

²⁹⁴ *Id.* at § (d)(1).

²⁹⁵ *Id.* at §§ (d)(2), (f).

²⁹⁶ *See, e.g.*, Council on Bioethics Report, *supra* note 100, at 177 (arguing that the FDA has no explicit legal authority to regulate on grounds of protection of a child resulting from ART as such).

foresee.²⁹⁷ Looking specifically at PHSA § 351, nothing in its language suggests that the FDA's mandate to ensure the safety and efficacy of biologics is limited only to DRT recipients or even just to "currently existing people." Moreover, there are examples of cases where the FDA asserted its regulatory authority over matters involving "future individuals," i.e. individuals not yet in existence when the treatment is carried out or the drug is administered. One prominent example is the FDA's prohibition on tests involving human cloning out of concern for the health of the future children that might be created by such a procedure.²⁹⁸ Furthermore, arguably at least in relation to the regulation of small molecule drugs (rather than biologics), in authorizing the FDA to require safety data analysis in relation to pregnant women, Congress granted the FDA the authority to tend to the safety of unborn children.²⁹⁹ At the very least, the abovementioned precedents indicate that it is not unreasonable for the FDA to construe its authority under PHSA § 351 broadly enough to encompass a role for itself in ensuring the safety of future individuals, including DRT children. Therefore, if the FDA were to construe its authority under PHSA § 351 as including the safety of DRT children, a court would most likely uphold that statutory construction under the *Chevron* doctrine.³⁰⁰

2. Lack of Authority to Regulate in the Area of Genetic Aspects of DRT

The issue of the FDA's authority to regulate the genetic aspects of DRT comes up also in a federal context as part of the question of the Federal Government's authority to

²⁹⁷ See Merrill, *supra* note 23, at 1 ("It is conventional wisdom that regulatory agencies possess discretion to interpret their program statutes in new ways in order to meet challenges that the congressional authors did not, and in many cases could not, anticipate . . . we have come to expect that agencies will often confront new challenges by adapting traditional tools, rather than reflexively returning to the legislature for new authority or instructions.").

²⁹⁸ For the FDA's controversial assertion of authority over human cloning due to concerns for the health and safety of individuals resulting from cloning procedures, see Letter from Stuart L. Nightingale, M.D., Associate Comm'r, FDA, to Inst. Review Boards 1 (Oct. 26, 1998), *available at* <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm150508.htm>. Another controversial example is the FDA's exceptional regulation of the drug thalidomide, known for its potential to cause severe birth defects out of concern for the unborn children. See generally Allen E. White, *Thalidomide and the FDA: Authority Overstepped or Legitimate Safety Measures?* (December 2001), *available at* <http://ssrn.com/abstract=294563>.

²⁹⁹ See 21 U.S.C. § 355(k)(3)(C)(iv)(I) (2009).

³⁰⁰ See *supra* note 292 (discussing the *Chevron* doctrine). Congress has clearly not addressed the matter of genetic aspects of DRT in PHSA and thus the question becomes whether a construction of PHSA that would require screening and testing of DRT donors for genetic diseases to ensure the safety of DRT children is a permissible construction of PHSA § 351. As argued above, such a construction is not only reasonable but also desirable. Assuming that courts would not find this view fundamentally inconsistent with the statutory language, they should uphold a construction of PHSA § 351 that would grant the FDA authority to regulate the genetic aspects of DRT.

regulate in the field of healthcare. DRT transactions routinely occur across state borders as well as over the Internet.³⁰¹ Accordingly, the Commerce Clause of the Constitution provides the FDA, via congressional delegation, the authority to regulate DRT.³⁰² Furthermore, it is quite possible that the federal power to regulate DRT also extends to intrastate commerce in DRT.³⁰³ Thus, the FDA has the authority under PHSA § 351 to regulate genetic aspects of DRT so long as traditional state regulatory prerogatives are not impermissibly impinged upon.

While the practice of medicine has traditionally been regulated by the states,³⁰⁴ the Supreme Court has recognized the ability of the federal government to set uniform national standards for health and safety.³⁰⁵ Thus, to the extent that FDA regulation of the

³⁰¹ See Gail Schmoller Philbin, *Web of Conception; Couples Turning to Internet Sites to Secure Donated Sperm*, Chicago Trib., Aug 20, 2003 at 1 (“While the Web has transformed the way couples . . . find donor sperm, it has also changed the way sperm banks do business.”); Don Oldenburg, *Sperm Banks Online: Going Too Far?* Wash. Post, Nov. 18, 1999, at C4. See also *OTA’s Infertility Report*, *supra* note 27, at 24 (“Sperm [is] sold by commercial sperm banks throughout the United States and [has] been for many years.”). In the absence of exact DRT sales’ statistics it is difficult to estimate the volume of interstate transactions in DRT and their percentage out of the total number of DRT transactions. However, it appears prudent to assume that a large portion of the DRT transactions occurring over the internet are not confined to within a single state’s borders. The prevalence of the use of the internet as well as several advantages the internet offers to DRT purchasers (e.g., privacy, a large selection of potential donors, ease of access), all increase the prevalence of the internet in DRT transactions, thereby presumably increasing the quantity of interstate DRT transactions both in general and as compared to intrastate DRT transactions.

³⁰² See U.S. Const. art. I, § 8, cl. 3; see also *OTA’s Infertility Report*, *supra* note 27, at 181-82 (discussing the use of the Commerce Clause to regulate in other fields of health care and medical laboratories).

³⁰³ At least on one occasion, a federal court upheld an FDA ban on intrastate commerce based on authority granted by PHSA § 361, recognizing that such a ban was reasonable to prevent the interstate spread of disease. See *Louisiana v. Mathews*, 427 F.Supp. 174, 176 (E.D. La. 1977). Notably, in so doing, the District Court for the Eastern District of Louisiana explicitly stated that “[i]t has long been established that businesses which affect interstate commerce may have their intrastate activities regulated.” *Id.* Thus, to the extent the regulation of intrastate commerce in DRT is necessary to prevent negative outcomes in interstate commerce, it is likely that the FDA could establish authority to regulate such intrastate commerce. Cf. *Wickard v. Filburn*, 317 U.S. 111 (1942) (holding that Congress’s power to regulate the production of wheat going into interstate commerce extends to wheat intended for personal use and not placed in interstate commerce.).

³⁰⁴ See Annas, *supra* note 22, at 938 (“[T]he regulation of medicine . . . [has] historically been dealt with under state law, not federal law.”); *Human Tissues and Organs*, *supra* note 104, at 15 (mentioning FDA’s policy of not regulating the practice of medicine).

³⁰⁵ *Gonzales v. Oregon*, 546 U.S. 243, 271 (2006) (internal citations omitted) (“Even though regulation of health and safety is primarily, and historically, a matter of local concern . . . there is no question that the Federal Government can set uniform national standards in these areas.”).

genetic aspects of DRT would touch upon the practice of medicine as some have argued,³⁰⁶ such regulation would be permissible³⁰⁷ and, at any rate, would not constitute a regulation of the practice of medicine any more than the well-accepted safety requirements of the Food, Drug and Cosmetic Act.³⁰⁸

Moreover, FDA regulation of the genetic aspects of DRT requiring the screening and testing of potential donors for genetic diseases would not directly impact the practice of medicine but would merely set the minimum safety standards for DRT intended for a *later* use by physicians. For example, it would not influence the interaction between physicians and their patients. Rather, the regulation would influence directly only the interaction between DRT institutions and practitioners with potential donors, and, *only later on*, affect DRT recipients. Admittedly, it is likely that some of the employees of DRT institutions are physicians and that in small institutions it might be the same physician who would harvest the DRT and then dispense it to patients. Yet, this fact does not automatically make the relationship between such physicians and donors a physician-patient relationship.³⁰⁹ Finally, to the extent that FDA regulation of the genetic aspects of DRT may impinge upon state regulation of the practice of medicine, it would do so no more than the FDA's existing regulation of the communicable diseases aspects of DRT.³¹⁰

³⁰⁶ When the FDA was just making its first steps into the regulation of DRT, professional organizations argued that it was "wading into the practice of medicine." *See FDA Tissue Practices Rule is Criticized by Industry, Physicians*, FDA Week, June 1, 2001, at 14. Yet, even those who criticized the FDA's intentions to regulate some of the transactions taking place between physicians and their patients agreed that regulation "at the sperm bank level" is justified and even desirable. *Id.*

³⁰⁷ Notably, an issue remains with respect to potential preemption of state laws by FDA regulation of the genetic aspects of DRT. However, this issue exceeds the scope of this Article.

³⁰⁸ *Cf. Merrill, supra* note 23, at 79 ("FDA has assumed oversight of other novel medical technologies and the common feature—use in the delivery of medical care—may lead to an assumption [that] Congress expects the agency to assume responsibility.").

³⁰⁹ *See Annas, supra* note 22, at 938 ("[T]o the extent that [ART] has become big business and to the extent that it is more accurately characterized as a commercial enterprise than as a medical or family-related enterprise, federal regulation of at least its interstate commercial aspects deserves consideration.").

³¹⁰ A requirement in federal regulation to screen and test donors for genetic diseases would not represent more interference in the practice of medicine or in the standards of practice upheld by the states than the similar federal requirements that are already in place with respect to communicable diseases. Furthermore, as stated by a former FDA official in the context of communicable diseases: "when one considers the obvious need to screen and test donors for communicable disease, [it makes] the practice of medicine issue less prominent." *Human Tissues and Organs, supra* note 104, at 11 (presentation of Stuart Nightingale, Associate Comm'r for Health Affairs, FDA). A similar argument could be made with respect to the screening and testing for genetic diseases.

3. The Difficulty in Defining “Genetic Diseases”

A conceptual difficulty that seems to haunt the discussion of genetic diseases is how to define the term “genetic disease.” This difficulty is twofold: in order to define “genetic disease” one must first define “disease”—an elusive concept which baffles healthcare professionals and policymakers. Second, one must generally characterize the phenotypes that fall within the boundaries of the concept of “disease.” The genetic context only complicates things further since many genetic traits cannot be characterized merely as either present or not-present but rather manifest themselves in many variations. For example, at what point (if at all) does one’s stature become debilitating enough to be considered a “disease?” And are conditions such as dwarfism and genetic deafness “genetic diseases” that justify exclusion of those having them from the DRT donor pool?³¹¹

These conceptual difficulties could pose a real obstacle to a regulation of the genetic aspects of DRT.³¹² Yet, regardless of whether the difficulties in defining “genetic diseases” played a role in the FDA’s decision not to regulate the genetic aspects of DRT, such difficulties should not serve as a justification for not pursuing regulation of this area. One does not have to be in possession of a clear and coherent definition of genetic diseases to determine that conditions such as Huntington’s disease and ADPKD are genetic diseases that should be screened out of any donor pool. As for those genetic conditions in which a decision is not as easy, the FDA could elect to rely on the judgment of professional organizations, expert bodies and the like to determine whether they warrant exclusion from the donor pool in promulgating its regulations.³¹³

4. Bioethical Issues

Another possible reason for the FDA’s avoidance of the genetic aspects of DRT is that regulation of this area would inevitably raise a variety of ethical issues.³¹⁴ As

³¹¹ See Robertson, *supra* note 222, at 441 (“Persons with disabilities are concerned about biases in genetic screening [and testing] programs that disfavor persons with disabilities.”); see also Martha A. Field, *Killing “the Handicapped”—Before and After Birth*, 16 Harv. Women’s L.J. 79 (1993); Erik Parens and Adrienne Asch, *The Disability Rights Critique of Prenatal Testing: Reflections and Recommendations*, 29(5) Hastings Center Report at S1 (1999) (laying out the disabled-rights criticism of genetic screening and testing).

³¹² See, e.g., Conrad, *supra* note 10, at 301-02.

³¹³ See *infra* note 336 (discussing the privatization of regulation). Notably, reliance on bodies of experts has been a widely used method for tackling complicated public policy issues. See, e.g., The Presidential Comm’n for the Study of Bioethical Issues, <http://www.bioethics.gov> (last visited Jun. 17, 2010). A possible advantage of such expert bodies is that they serve as a “black box”—a socially acceptable decision-making method which is especially suited for issues that spur social controversy.

³¹⁴ Such issues may include the following: which genetic diseases (if any) should render a candidate ineligible to become a donor? How much choice should potential parents have in

recognized by several scholars, executive agencies are known to be averse to regulating matters that raise bioethical issues, especially in the context of ART, and therefore tend to refrain from regulating such matters to the extent possible.³¹⁵ Others have suggested that the FDA might be trying to avoid the regulation of DRT because it wishes to prevent a hijacking of the regulatory process by interest groups wishing to promote their ethical preferences.³¹⁶ Thus, it is conceivable that in avoiding the regulation of genetic aspects of DRT the FDA might have actually been trying to avoid the bioethical issues involved, thereby passing this hot potato along to others, e.g., professional organizations, state courts and expert commissions.

If this is indeed the case, the FDA might be throwing the baby out with the bath water because in so doing it foregoes an opportunity to regulate aspects of this area that do not raise difficult ethical issues.³¹⁷ Moreover, as discussed earlier with relation to the European model of regulation of DRT, it is possible to maintain the safety of DRT children without compromising ethics by deferring to and adopting into its regulation “ready-made” practical and ethical solutions devised by other authoritative institutions

choosing the traits of their offspring? Who should have access to a candidate’s genetic data or to that of her family members which she has unavoidably disclosed as part of the screening and testing process? See Robertson, *supra* note 222, at 457-459 (addressing the impact of screening and testing on offspring and arguing that screening and testing are a “private” form of eugenics that is permissible); Terra Ziporyn, ‘Artificial’ Human Reproduction Poses Medical, Social Concerns, 255 JAMA 13, 14 (1986) (describing issues related to donors’ privacy).

³¹⁵ According to the President’s Council on Bioethics, “[t]he appeal of doing nothing in [the area of ART] is, frankly, rather great, not only because the costs of regulation may be high . . . but also because the areas of assisted reproduction, new genomic knowledge, and embryo research are socially and politically quite sensitive.” Council on Bioethics Report, *supra* note 100, at 185; see also Eugene Bardach & Robert A. Kagan, Going by the Book: The Problem of Regulatory Unreasonableness 48-49 (1982) (arguing that “[r]egulatory officials . . . often are grateful for the opportunity to escape responsibility for the intellectually difficult and politically touchy task of making [risk vs. social benefit] trade-off decisions” and quoting former FDA commissioner, Donald Kennedy statement that “[f]ortunately, our statute does not allow us to weigh adverse health conditions against dollars”); Annas, *supra* note 22, at 937 (arguing that the United States has been slow to regulate the ART industry because of bioethical controversies); Judith Daar, *Regulating Reproductive Technologies: Panacea or Paper Tiger?*, 34 Hous. L. Rev. 609, 639 (1997) (suggesting that the lack of regulation of ART is a result, at least in part, of the fact that this area is politically charged).

³¹⁶ See Merrill, *supra* note 23, at 63 n.332 (“It is possible, perhaps even likely, that FDA was reluctant to acknowledge its authority to regulate a set of procedures that have excited intense interest, considerable controversy, and wide publicity . . . if the Agency were to enter the [area of assisted reproductive services], it would surely face pressure from opponents of many of these services to go much further than ‘mere’ public health concerns might lead it to go.”).

³¹⁷ For example, the merits of requiring the screening and testing of potential donors for ADPKD, Tay-Sachs and other lethal genetic conditions is not controversial.

such as professional organizations.³¹⁸ Thus, hypothetically, if the FDA were to regulate the genetic aspects of DRT it could use practice guidelines and professional standards for determining which conditions should be screened and tested for. In this way, the FDA could remain within its element—the safety of DRT recipients and DRT children—and avoid the need to address specific bioethical issues while deferring to and benefiting from thoughtful solutions devised by professionals, which usually reflect careful balances struck through a significant investment of resources and expertise.

5. Cost Considerations

Arguably, regulation of the genetic aspects of DRT would impose such costly requirements that it might make DRT more, and possibly even prohibitively, expensive for some potential DRT recipients.³¹⁹ This might not only cause many DRT institutions to go out of business³²⁰ but also may encourage many potential consumers who would no longer be able to afford to pay for DRT to seek other, less strictly regulated sources of DRT (e.g., abroad) or even forego the option of using DRT altogether.

Although there is no current estimate of the costs of applying the genetic screening and testing schemes recommended by the ASRM and AATB, it is possible to estimate the cost of such screening and testing. First, all of the states fund programs for the genetic testing of newborns for various genetic conditions that, with proper care, could be treated if diagnosed at an early stage.³²¹ New York State, for example, runs a Newborn Screening Program that performs over eleven million tests annually and tests

³¹⁸ Choosing this course of action may give rise to constitutional issues having to do with the delegation of FDA power to private entities. See *infra* note 336.

³¹⁹ Requiring the routine testing of every potential DRT donor for various conditions could result in a considerable increase in the costs involved in the processing of DRT.

³²⁰ The most costly elements of regulation of the genetic aspects of DRT would probably be the heightened screening and testing requirements. There are a few other possible costs involved in such regulation, e.g., costs involved in inspection and complying with inspection requirements, costs involved in appropriate recordkeeping, costs of communicating adverse events, etc. Yet, it appears that such costs would be very low, if not nominal. For example, the FDA estimated the costs related to being subject to periodic inspections at approximately \$768 per establishment per inspection. See 69 Fed. Reg. 68663 (FDA Nov. 24, 2004).

³²¹ See Nat'l Newborn Screening & Genetic Resource Ctr., State Map Page, <http://genes-r-us.uthscsa.edu/resources/consumer/statemap.htm> (last visited May 9, 2010). For a list of genetic conditions for which newborns are tested, see the National Newborn Screening Status Report (July 7, 2009), available at <http://genes-r-us.uthscsa.edu/nbsdisorders.pdf>. The existence of such genetic testing programs funded by all of the states also seems to reinforce the arguments in favor of genetic testing of DRT donors. Specifically, if it is justifiable to conduct genetic testing *after* a child is born, then it is even *more justified* to screen beforehand, i.e. prior to the actual manifestation of the genetic risk which arguably occurs at the moment of conception. In other words, genetic testing of DRT donors is a true preventative measure while newborn screening could at best guarantee appropriate treatment of an existing and irreversible genetic condition.

over a quarter of a million newborns a year for more than forty genetic conditions as well as HIV and congenital hypothyroidism.³²² The annual cost of all of the testing done by the New York Program is \$11.9 million.³²³ Second, numerous private laboratories offer various genetic testing products and services: for as little as \$25, parents and physicians may acquire kits or sets of genetic tests.³²⁴ For instance, the University of Colorado offers a kit that tests for twenty disorders recommended by the American College of Medical Genetics (ACMG) for \$25,³²⁵ another private laboratory offers testing for about fifty genetic conditions for \$199.³²⁶ Third, some laboratories also offer *prenatal* genetic screening. For example, for a price of \$1,850, one private laboratory offers genetic testing of fetuses based on DNA chip technology that evaluates over 2,100 DNA sequences associated with over 100 genetic syndromes.³²⁷ These figures suggest that the average cost of genetic testing for a given genetic mutation could be estimated at about \$1-3, depending on the technology used. Thus, under a rough estimate, it is not unreasonable to expect that the genetic testing of potential DRT donors in accordance with professional guidelines would cost several hundreds of dollars per donor.³²⁸

³²² See Wadsworth Center Newborn Screening Program, <http://www.wadsworth.org/newborn/index.htm> (last visited May 9, 2010).

³²³ Electronic mail letter from Deborah Rodriguez, Newborn Information Coordinator, Wadsworth Center, to author (July 21, 2009) (on file with author). Based on these figures it is possible to roughly calculate the cost of testing at about \$47.6 per newborn and \$1.08 per test.

³²⁴ See, e.g., Save Babies Through Screening Foundation, A Parent's Guide to Newborn Screening 2 (May 2005), *available at* <http://www.savebabies.org/library/HandoutAParentsGuidetoNBS.pdf>.

³²⁵ See Univ. of Colorado Health Sciences Ctr., Expanded Newborn Screening Program, <http://www.uchsc.edu/newbornscreening/index.htm> (last visited May 9, 2010).

³²⁶ See PerkinElmer Genetics, Order StepOne®, <http://www.perkinelmergenetics.com/OrderScreeningPacket.htm> (last visited May 9, 2010). For a list of the genetic conditions tested for, see <http://www.perkinelmergenetics.com/DisordersScreened.htm> (last visited Jun. 17, 2010).

³²⁷ See The President's Council on Bioethics, The Changing Moral Focus of Newborn Screening 80 (2008) [hereinafter *Changing Moral Focus*] *available at* http://bioethics.georgetown.edu/pcbe/reports/newborn_screening/index.html. See also Signature Genomic Laboratories, Signature PrenatalChip®, <http://www.signaturegenomics.com/prenatalchip.html> (last visited May 9, 2010).

³²⁸ This estimate is based on the assumption that professional guidelines would require testing for a few hundred known genetic mutations and that the cost of testing for each individual mutation is, as mentioned above \$1-3. It is probably also safe to assume that, in the future, as testing technologies advance and become more commonplace, genetic testing of DRT donors would become cheaper. It is anticipated that by 2014, the sequencing of an entire human genome would cost only about \$1,000. See *Changing Moral Focus*, *supra* note 327, at 52. Analysis of an entire individual's genome would make it possible to analyze the genome of such individual for

It is important to note that not all potential DRT donors should be subject to such extensive testing; only the most promising candidates who make it through vigorous initial screening based on a physical examination and thorough questioning would merit such expenditure. Thus, even if we assume that such extensive genetic testing of potential DRT donors would impose additional costs on DRT institutions and—by way of roll over—recipients, it is expected that such additional costs and expenditure would not make DRT significantly more costly or less accessible than it already is.³²⁹

Moreover, if one is to accept the picture of institutional compliance with professional guidelines among DRT institutions portrayed by the FDA, it may well be that regulating the genetic aspects of DRT would not substantially affect the DRT industry. According to the FDA, the twenty largest DRT institutions that account for 95% of the DRT industry already screen and test potential DRT donors in accordance with professional guidelines.³³⁰ Thus, presumably, regulations requiring compliance with professional standards as they pertain to genetic aspects of DRT would not impose additional costs on most DRT transactions. Rather, such regulations would only affect DRT institutions that do not already follow professional guidelines and recipients purchasing DRT from such institutions.³³¹

Another aspect of the costs involved in regulating the genetic aspects of DRT is the costs that such regulation would impose on the FDA itself. Agencies' ability and willingness to regulate are closely linked to the financial burden that the regulation would impose on their limited resources. Yet, the cost of regulation to agencies often tends to be

all the genetic mutations known without having to resort to costly and cumbersome specific testing for specific genetic conditions, as is done now.

³²⁹ With each sperm sample sold at a few hundreds of dollars and under the assumption that each sperm donor would be the source of at least dozens of samples, it may be assumed that the additional cost of extensive genetic testing would not significantly contribute to the cost of sperm. The cost of egg donations, on the other hand, is already so high, that arguably, the additional cost of proper genetic testing of potential donors is not expected to change it significantly.

Notably, the area of DRT raises numerous issues related to the accessibility of DRT and related services to different income groups. DRT in general and egg donations in particular are expensive propositions and, as such, are more available to individuals and families with higher income and/or better medical insurance coverage that includes DRT and related services. Yet, given the above conclusion that proper genetic screening and testing of DRT is not expected to make DRT and related services significantly more expensive, it is also not expected that it would push DRT and related services further beyond the reach of lower income groups.

³³⁰ According to the FDA, those institutions that were in compliance with AATB standards would have felt minimal impact as a result of the FDA Final Donor Eligibility Rule, while the remaining 90 smaller institutions examined, which accounted for 5% of the industry, "[would] be more significantly affected." *See FDA Final Donor Eligibility Rule*, *supra* note 24, at 29819.

³³¹ Regulatory requirement of genetic screening and testing that conforms to professional guidelines would therefore prevent a possible market failure where such non-compliant DRT institutions externalize the costs involved in appropriate screening and testing to DRT recipients and DRT children in the form of heightened risk.

overlooked.³³² However, given that the FDA is already involved in the regulation of DRT and inspection of DRT institutions, applying the FDA's Human Tissue Regulations' framework to genetic aspects of DRT should not create a substantial additional financial burden for the FDA.³³³

Finally, in performing the cost-benefit analysis in the context of genetic screening and testing of DRT, it is imperative to consider the possible long-term benefits that mandatory testing requirements may have on future healthcare expenditure on a societal scale.

In conclusion, the regulation of the genetic aspects of DRT is likely to raise conceptual and bioethical issues and impose at least some additional costs on DRT institutions and recipients. Yet, these obstacles are not unique to this area of regulation and should not deter the FDA. Furthermore, as demonstrated above, FDA regulation of the area of genetic aspects of DRT could rely on solid legislative and constitutional grounds. Accordingly, such regulation is not only desirable but also feasible.

C. Some Recommendations for FDA Regulation of the Genetic Aspects of Donated Reproductive Tissue

As mentioned earlier, this article does not purport to suggest exactly what FDA regulation of the genetic aspects of DRT should look like and what it should include; these issues are best left to the expertise of the FDA and DRT professionals. However, it is possible to enumerate key elements that such regulation should include.

Perhaps the most important purpose of regulation of the genetic aspects of DRT should be ensuring the health and safety of DRT children rather than just those of DRT recipients and donors.³³⁴ Just as in the context of communicable diseases, the regulation should be based on an understanding that the mere fact that a disease might occur in the general population—which does not have its reproductive cells and tissues screened and

³³² It is not unfathomable that one of the reasons that the FDA has not regulated the genetic aspects of DRT is simply a lack of resources. For example, according to an FDA official, lack of manpower and resources to regulate sperm banks was the underlying reason for allowing self-regulation in the area of DRT. *See Human Tissues and Organs, supra* note 104, at 23-24 (“[S]ince basically the entire scientific staff and other personnel devoted to sperm banking was myself about half-time, and because the American Association of Tissue Banks had been formed at the same time, we decided that we would maintain a liaison with AATB and allow voluntary standards to be used in the area of semen banking.”). According to Merrill, the FDA appears to “confront more than its share of novel challenges” and thus may have to decide how to distribute its limited resources more frequently than other agencies. *See Merrill, supra* note 23, at 2.

³³³ *See Merrill, supra* note 23, at 80 (characterizing the FDA's Human Tissue Regulations as striking “a reasonable balance between public health protection, on the one hand, and the constraints of its own budget and tissue bank resources on the other”).

³³⁴ *See Council on Bioethics Report, supra* note 100, at 217.

tested—does not justify not taking measures to avoid it in DRT children.³³⁵ Thus, in regulating the genetic aspects of DRT, the FDA should strive to ensure that DRT institutions take all reasonable measures to prevent and avoid the occurrence of genetic diseases in DRT children.

In promulgating regulations addressing the genetic aspects of DRT, especially in the context of screening and testing requirements, the FDA should consider the recommendations and guidelines of professional organizations.³³⁶ As explained above, the FDA could greatly benefit from the accumulated knowledge, experience and thinking in professional organizations and from solutions they have come up with through years of dealing with the issues that are going to become the focus of regulation. By relying on professional standards, the FDA would not only ensure that its regulatory scheme is always reasonably up-to-date and relevant but also preserve the financial and political

³³⁵ See Ziporyn, *supra* note 314, at 14 (quoting Lori Andrews' argument that the position that there is no need to test DRT donors for medical and genetic defects because "normal" couples do not always undergo genetic testing before conception is "unscientific and unethical"); see also *supra* Part II.E.

³³⁶ See Council on Bioethics Report, *supra* note 100, at 217 (recognizing that professional oversight has traditionally been the principal mechanism of regulation for the practice of medicine). Notably, coordination with the recommendations and guidelines of professional organizations coincides with the FDA's own preferences with relation to the regulation of human tissue. See Zoon Statement, *supra* note 59, at 105 ("In the future . . . FDA intends to use various venues to continue our dialogue with industry organizations such as the AATB . . . [and] the American Society for Reproductive Medicine (ASRM)/Society or [*sic*] Assisted Reproductive Technology (SART).").

Importantly, deferment to and reliance on standards set by professional organizations raises the issue of "privatization as delegation." See generally Gillian Metzger, *Privatization as Delegation*, 103 Col. L. Rev. 1367 (2003). According to Metzger, when private entities "wield substantial power over government programs and their participants," the government effectively delegates power to such private entities in a manner that might undermine "constitutional accountability." *Id.* at 1376-77. Metzger argues that for such delegation of government power to private entities to be constitutional it must be sufficiently constrained, e.g., by ensuring government supervision over the private entities' decision-making by creating a complaint or appeal system through which affected third-parties could challenge specific decisions, policies and procedures of the private entities that affect them. *Id.* at 1471-72. Arguably, per Metzger, FDA reliance on and deferment to professional guidelines (such as those of the AATB and ASRM) in the context of regulation of genetic aspects of DRT could constitute a delegation of government power to private entities because it may effectively enable such entities to act on behalf of the government in formulating professional standards of practice for third parties, i.e. DRT institutions. *Id.* at 1462. Accordingly, in order to ensure that such reliance on professional guidelines is endowed with sufficient constitutional accountability, the FDA could include in the regulations addressing the genetic aspects of DRT a mechanism that would enable DRT institutions affected by professional guidelines to challenge the inclusion of a particular guideline or standard in the regulations. Notably, such a mechanism, the Tissue Reference Group (TRG) has already been established in the Human Tissue Regulations to resolve disputes arising from implementation of these regulations. See 66 Fed. Reg. 5451 (FDA Jan. 19, 2001) (comment 7).

resources that it would otherwise need to expend on tackling complicated bioethical issues.³³⁷

As for the screening and testing of potential donors, the FDA could rely on a protocol similar to the one it already employs in its Human Tissue Regulations, which requires, among other things, the collection of relevant medical records, including a donor's medical history and physical examination report.³³⁸ The FDA should also require the collection of as detailed a family medical history as possible and its use to identify risk factors that may prompt further specific testing beyond that which would be required from every donor or from donors belonging to particular ethnic groups.³³⁹

The FDA regulations should set up a national record-keeping system that includes information on all donors nationwide. The database should assist in keeping track of the number of DRT children born from each donor's gametes and include the medical history of donors, their contact information and adverse events in DRT children as they pertain to genetic conditions. Such a database could assist in avoiding procreation between blood-related DRT children.³⁴⁰ Even more importantly, it would ensure that DRT suspected of causing adverse effects is not used again and that the donor is not permitted to donate any more DRT anywhere in the country before the source of the genetic problem is verified.³⁴¹

Finally, as recommended by the GAO, the FDA regulations should require that prospective DRT recipients be made aware and receive an explanation of relevant genetic

³³⁷ See *supra* Part IV.B.4.

³³⁸ See FDA's *Guidance for Industry Announcement*, *supra* note 50, at 12-14.

³³⁹ Identifying risk factors and assessing them are also required by the FDA with respect to communicable diseases. See *id.* at 15.

³⁴⁰ See Cohen, *supra* note 23, at 363.

³⁴¹ Such a database would have helped in preventing cases such as that of the Michigan donor whose sperm was used for conceiving 11 children, five of whom were later found to have an extremely rare type of leukemia. See Denise Grady, *Sperm Donor Seen as Source of Disease in 5 Children*, N.Y. Times May 19, 2006, at A16. According to experts, this particular genetic defect, which is passed along by an autosomal dominant gene, would probably not have been picked up as part of a regular screening and testing protocol. *Id.* However, a database would have enabled reporting of the discovery of the first case of leukemia in the donor's progeny, thereby not only alerting other recipients (through their DRT institutions) regarding possible risks to their DRT children, but also ensuring that DRT institutions did not further use the compromised donor's DRT. Cf. Daar & Brzyski, *supra* note 15, at 1703 (calling for the institution of a national gamete donor registry to avoid such cases as the recently reported transmission of potentially lethal heart defect by a sperm donor to 9 out of 24 children conceived using his sperm, including the donor's own child); Maron et al., *supra* note 5, at 1681-83 (reporting a case where a donor transmitted a unique genetic condition causing a lethal heart defect to at least 9 out of 24 children conceived from his sperm, including one of his own two sons, recommending assembling and sharing clinical data for all individuals born from the same donor's DRT and emphasizing the importance of notifying gamete donors, recipients, and other affected parties about the occurrence of genetic diseases).

data of potential donors in accordance with existing informed consent standards. DRT recipients should also be advised about the types of genetic testing, if any, performed on any particular DRT and the potential risks of genetic diseases embodied in that particular DRT as compared to the level of risk in the general population.³⁴² In this manner, the FDA regulations would not only ensure that DRT recipients only use genetically compromised DRT *after* making an informed choice but also that they are made aware of the possible monetary and legal ramifications of such a choice.³⁴³

V. CONCLUSION

Three decades have passed since Curie-Cohen published the results of a survey revealing significant deficiencies in the practices of genetic screening and testing of sperm and yet, children born from donated reproductive tissue, whether sperm or ova, are still exposed to unnecessarily high levels of genetic risk. Despite ongoing efforts by professional organizations, the extent of self-regulation of the donated reproductive tissue industry is unclear and its effectiveness is questionable. Accompanied by inconsistent state regulation of the reproductive tissue industry and non-detering relief afforded by

³⁴² Enforcing such a requirement would put DRT recipients in the place of other couples who undergo prenatal medical screening and testing for genetic diseases prevalent in their ethnic group and would enable them to make their own decision whether they wish to use the DRT at the risk of passing an identified genetic condition to their DRT child, forego the use of the particular DRT or utilize pre-implantation genetic diagnosis (PGD) to test their embryo. *See* Robertson, *supra* note 222, at 456-57 (describing the different possible choices prospective parents have); *see also* GAO 1997 Report, *supra* note 182, at 31 (“We recommend that the Secretary . . . direct FDA to take action in several areas to improve the safety of [DRT] and to increase FDA’s ability to regulate tissue facility activities . . . FDA should also add to its oversight plans provisions that would require . . . disclosure of genetic tests that have been performed on donated reproductive tissue.”). Interestingly, in its response to the GAO 1997 Report, the FDA agreed with these requirements. *See* Letter from Diane E. Thompson, Associate Commissioner for Legislative Affairs, DHHS, to Bernice Steinhardt, Director, HEHS, GAO (Oct. 23, 1997) (“In general, FDA agrees that recipients of tissue should know, through appropriate labeling of the tissue, the results of testing performed. Ethical, scientific and regulatory issues regarding genetic tests are currently under discussion within the Department of Health and Human Services in connection with the final report of the Task Force on Genetic Testing.”). Notably, the report of the Task Force on Genetic Testing mentioned in the FDA’s response does not mention the genetic screening or testing of DRT. *See* Final Report of the Task Force on Genetic Testing (Neil A. Holtzman and Michael S. Watson eds. 1997), available at <http://www.genome.gov/10001733>.

³⁴³ Some of the ramifications of choosing to use genetically-compromised DRT could include, for example, an implied waiver of possible claims against professionals involved in the preparation, distribution and use of the DRT. Requiring disclosure and informed consent with respect to genetic conditions that might be passed along by particular DRT would also provide adequate response to any concerns regarding the reproductive freedom of recipients. *See* Robertson, *supra* note 222, at 457 (“[W]anting information about the genetic makeup of prospective offspring and then acting on it fits squarely within conventional understandings of procreative liberty.”).

the courts in matters involving children born from genetically defective donated reproductive tissue, the genetic safety of individuals born from such tissue is a cause for concern.

This Article described only a handful of publicized tragedies that befell children born from genetically defective reproductive tissue and their families. There is no way of knowing how many more such cases actually occurred, and yet, without a fundamental change in the regulation of donated reproductive tissue to address genetic risks involved in the use of such tissue, more tragedies are very likely to occur. As we accumulate knowledge about human genetics and develop more diagnostic means to test for and possibly prevent the transmission of genetic diseases through donated reproductive tissue, the need for regulation will only become more accentuated. Furthermore, without appropriate regulation, the growing demand for donated reproductive tissue will further increase the genetic risks involved in the use of donated reproductive tissue.

As recognized by the FDA, non-involvement of the federal government in the area of donated reproductive tissue jeopardizes the safety of the public. Thus, at least as a matter of public health policy, the FDA's distinction between communicable diseases and genetic diseases in the context of donated reproductive tissue cannot be justified. The Public Health Service Act endows the FDA with ample authority to regulate all aspects of donated reproductive tissue and provides it with all the tools necessary to ensure the safety of recipients of such tissue and their children. Indeed, the regulation of genetic aspects of donated reproductive tissue would undoubtedly raise difficulties resulting, for example, from bioethical issues involved in this area and the need to carefully balance costs against potential benefits. However, overcoming such difficulties is well within the capabilities of the FDA.

Furthermore, regulations addressing the genetic risks involved in the use of donated reproductive tissue could offer "a unique opportunity to reduce or even eliminate genetic risks,"³⁴⁴ which would benefit generations to come. Unfortunately, it appears that the regulation of genetic aspects of donated reproductive tissue is not on the FDA's "to do list."³⁴⁵ Hopefully, renewed interest in the regulation of sectors that are not sufficiently self-regulated will prompt the FDA to supplement its current regulation so as to also address the genetic aspects of donated reproductive tissue.

³⁴⁴ See Conrad, *supra* note 10, at 298.

³⁴⁵ In its June 2007 report, the FDA's Human Tissue Task Force listed numerous "recommendations that may be implemented with additional planning and/or resources," which would improve the breadth and depth of the FDA's Human Tissue Regulations. However, these recommendations did not include addressing genetic aspects of DRT. See HTTF Report, *supra* note 67, at 7.

Patents vs. Statutory Exclusivities in Biological Pharmaceuticals—Do We Really Need Both?

I. Introduction

Over the past decade or so, the United States has been the arena of a boisterous debate regarding the institution of a regulatory framework for the approval of generic versions¹ of biologics-based pharmaceutical products (also known as “biological products” and “biologics”²)³—an important and increasingly growing class of drugs.⁴ The basic premise of

¹ In this Article, the terms “generics” or “generic versions” will be used to refer to imitations and follow-on versions of already approved drug products, which are the subject of an application for marketing submitted to the FDA. Applications for generic versions of drug products typically attempt to rely on FDA findings of safety and efficacy reached as part of its review of the already approved version of the relevant drug product.

Notably, the term “generic biologics” in and of itself has spawned a considerable amount of controversy as the nomenclature in the area of biologics seems to be perceived as dictating the discussion’s results. *See e.g.* Henry G. Grabowski, David B. Ridley & Kevin A. Schulman, *Entry and Competition in Generic Biologics*, 28 *Managerial and Decision Economics* 439 n. 2 (2007), available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=992479 (asserting that while “[t]hroughout the paper we refer to ‘generic biologics’ for the sake of symmetry with generic pharmaceuticals[,] the term ‘follow-on biologic’ might be more appropriate, . . . given that the product might be required to complete clinical trials to demonstrate similar safety and efficacy to the originator”); Wendy H. Schacht & John R. Thomas, CRS Report for Congress: Follow-On Biologics: Intellectual Property and Innovation Issues, at 3 (2008) [hereinafter 2008 CRS Report] (“many experts do not describe competing biologic products as “generics,” as is the case for small-molecule pharmaceuticals; the term “follow-on biologic” is commonly used instead”); Follow-On Protein Products: Hearing before the Committee on Oversight and Government Reform, 110th Cong., 3 (March 26, 2007) (statement of Janet Woodcock, M.D., Deputy Commissioner, Chief Medical Officer, FDA), available at <http://www.hhs.gov/asl/testify/2007/04/t20070326a.html> [hereinafter Woodcock Statement] (addressing the issue of terminology and explaining why she prefers the term ‘follow-on protein products’). The particular term used in the context of the new healthcare reform act to indicate an imitation of an already approved product is “biosimilar” (rather than “biogeneric,” “generic biologic,” “follow-on biologic,” “generic biological product,” etc.). However, given the genericity of the term “generic” to the legal discussion of regulated imitation-products and its wide use in the context of drug law, in this Article I will use the term “generic” as mentioned above.

² The FDA defines biological products as “any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention, treatment or cure of diseases or injuries of man.” *See* 21 C.F.R. § 600.3(h). According to the FDA Center for Biologics Evaluation and Research (CBER),

Biological products include a wide range of products such as vaccines, blood and blood components . . . somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources - human, animal, or microorganism - and may be produced by

such a framework is the creation of a fast and less-costly route to FDA approval for biologics that would be similar or identical to already-approved biological products—typically ones that

biotechnology methods and other cutting-edge technologies . . . Biological products often represent the cutting-edge of biomedical research and, in time, may offer the most effective means to treat a variety of medical illnesses and conditions that presently have no other treatments available.

...

In contrast to most drugs that are chemically synthesized and their structure is known, most biologics are complex mixtures that are not easily identified or characterized. Biological products, including those manufactured by biotechnology, tend to be heat sensitive and susceptible to microbial contamination. Therefore, it is necessary to use aseptic principles from initial manufacturing steps, which is also in contrast to most conventional drugs.

FDA CBER, What are “Biologics” Questions and Answers, <http://www.fda.gov/AboutFDA/CentersOffices/CBER/ucm133077.htm> (“CBER FAQ”); *see also* the Public Health Service Act (PHSA) ch. 373, 58 Stat. 682 § 351(i) (1944) (codified as 42 U.S.C. § 262(i)): (“the term ‘biological product’ means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings.”). Accordingly, in this Article, I will use the terms “biologics” and “biological products” to refer to pharmaceutical products whose manufacturing involves the use of living organisms and will distinguish them from “small molecule drugs” (or “drugs” for short). For further discussion of the differences between biologics and small molecule drugs and the possible implications of these differences on frameworks for the approval of generic versions of biological products, *see generally* Donna M. Gitter, *Innovators and Imitators: An Analysis of Proposed Legislation Implementing an Abbreviated Approval Pathway for Follow-On Biologics in the United States*, 35 Fla. St. U. L. Rev. 555, 560 (2008); Bryan A. Liang, *Regulating Follow-On Biologics*, 44 Harv. J. on Legis. 363, 367-378 (2007); Biotechnology Industry Organization (BIO), *The Difference with Biologics: The Scientific, Legal, and Regulatory Challenges of Any Follow-On Biologics Scheme*, 6-8 (2007), <http://www.bio.org/healthcare/followonbkg/WhitePaper.pdf> [hereinafter BIO White Paper].

³ *See generally* Tam Q. Dinh, *Potential Pathways for Abbreviated Approval of Generic Biologics Under Existing Law and Proposed Reforms to the Law*, 62 Food & Drug L.J. 77 (2007) (discussing the debate regarding the FDA’s authority to create an abbreviated regulatory pathway for the approval of generic versions of biological products); Jeremiah J. Kelly & Michael David, *No Longer “If,” but “When”: The Coming of Abbreviated Approval Pathway for Follow-On Biologics*, 64 Food & Drug L.J. 115, 116 (2009) (reviewing the history of the debate over a U.S. regulatory scheme for the approval of generic biologics).

⁴ *See generally* Robert J. Shapiro et al., *The Potential American Market for Generic Biological Treatments and the Associated Cost Savings*, at 1-3 (2008), *available at* http://www.sonecon.com/docs/studies/0208_GenericBiologicsStudy.pdf (describing the importance of biologics as a class of drugs, the growing numbers of biological products, important research done in the area of biologics and their economic impact); 2008 CRS Report, *supra* note 1, at 1-2 (discussing the importance of biologics as a class of drugs); Liang, *supra* note 2, at 363-64 (describing the prominence of biologics in the worldwide drug market). The importance of biologics lies in their structural and functional variety which, in turn, embodies unprecedented therapeutic promise. Already, approved biologics include “wonder drugs” used to treat diseases and maladies that could not be treated effectively by small-molecule drugs and in many cases used to be considered fatal. Examples of biologics include anti-cancer antibodies such as Herceptin and Avastin, anti-arthritis products such as Enbrel and Remicade, insulin products such as Humulin for the treatment of diabetes, erythropoietin products such as Procrit, clotting factor VIII for the treatment of hemophilia and Aranesp for the stimulation of growth of red blood cells in people suffering from blood disorders such as anemia.

are sold on the market at monopoly rates—thereby allowing for cheaper versions of such medicines to enter the market. One of the main points of contention in creating the framework for the approval of generic biologics has had to do with the length of the exclusivity period that would be granted to developers of original biologics during which generic competitors would not be allowed to enter the market.⁵ On March 21, 2010, as part of the healthcare reform, Congress

⁵ Since the imposition of competition on a previously monopolized market is expected to be accompanied by a drop in the price of the biological product, it is in the best interest of the monopolist to make its monopoly period as long as possible. There are a variety of positions on the appropriate length of the period of such exclusivity. Different proposals raised over the past few years proposed setting the length of exclusivity period, in years, at 0, 3-6, 7, 10, 12-12.5, 12-14.5, 12-15, 13-16, 17, etc. See Gitter, *supra* note 2, at 615-616 (reviewing different positions on the length of exclusivity period that should be afforded to original biological products); Henry Grabowski, *Follow-on Biologics: Data Exclusivity and the Balance Between Innovation and Competition*, 7 *Nature Reviews Drug Discovery* 479, 486 (2008) [hereinafter Grabowski 2008] (advocating a data exclusivity period of 12.9-16.2 years); Henry Grabowski, Genia Long & Richard Mortimer, *Data Exclusivity Periods for Biologics: Updating Prior Analyses and Responding to Critiques*, http://econ.duke.edu/Papers/PDF/Data_Exclusivity_Periods_for_Biologics.pdf, at 2, 30 (2008) (reiterating Grabowski's call for a 12-16 year exclusivity period) [hereinafter Grabowski et al.]. Laurence J. Kotlikoff, *Stimulating Innovation in the Biologics Industry: A Balanced Approach to Marketing Exclusivity* (2008) (arguing that granting developers of original biologics exclusivity periods of 12-15 years would create too long monopoly periods that will distort the economy of pharmaceuticals and calling for limiting exclusivity periods in biologics to lengths such as those granted under the Hatch-Waxman Act); Alex M. Brill, *Proper Duration of Data Exclusivity for Generic Biologics: A Critique*, at 11 (2008), available at http://www.tevadc.com/Brill_Exclusivity_in_Biogenics.pdf (bringing a critique of Grabowski's determination that the proper data exclusivity period should be 12.9-16.2 years and arguing that under a "more plausible set of circumstances," the proper data exclusivity period should be around ten years); Henry Grabowski & Joseph DiMasi, *Biosimilar, Data Exclusivity, and the Incentives for Innovation: A Critique of Kotlikoff's White Paper*, http://econ.duke.edu/Papers/PDF/FinalDraft2_5_09.pdf, at 4-5 (2009) (criticizing Kotlikoff's argument against granting a 12-15 year data and/or exclusivity period) [hereinafter Grabowski & DiMasi 2009]; *Teva Discusses Follow-On Biologics, Initiatives for 2009*, 8 *Drug Industry Daily*, Feb. 11, 2009 (discussing Teva's call for a 7 year exclusivity period); Henry Grabowski, *Data Exclusivity for Biologics: What Is the Appropriate Period of Protection?*, American Enterprise Institute for Public Policy Research (AEI)—Public Policy Outlook No. 10 (2009) [hereinafter Grabowski 2009] (reiterating his position, as expressed in previous articles, that the minimum period of exclusivity should be set at twelve years); Biotechnology Industry Organization (BIO), *A Follow-On Biologics Regime Without Strong Data Exclusivity Will Stifle the Development of New Medicines*, at 1 (2007) [BIO Data Exclusivity Position Paper] (advocating a data exclusivity period for biologics of "no less than 14 years"); John A. Vernon, Alan Bennett & Joseph H. Golec, *Exploration of Potential Economics of Follow-on Biologics and Implications for Data Exclusivity Periods for Biologics*, B.U. J. Sci. & Tech. L. 55 (2010) ("there should be 17 years of [] exclusivity for new biologics."). See also *infra* note 71. But see Federal Trade Commission, *Emerging Health Care Issues: Follow-on Biologic Drug Competition*, at v-vii (2009) [hereinafter FTC Report] (recommending against granting statutory exclusivity in biological products in addition to existing patent protection and determining that it is likely that generic competition in biologics will develop without any special legislative incentives).

Notably, in Europe, original biological products are afforded a 10-11-year statutory exclusivity consisting of 8 years of data exclusivity during which it is not possible to file applications for generic versions of the biological product, two more years of market exclusivity, during which generic applications cannot be approved, and an

settled this debate by passing the Biologics Price Competition and Innovation Act of 2009 ('BPCIA'), which provides statutory exclusivity⁶ periods of 12-12.5 years for original biologics from the date of FDA approval.⁷ This 12-12.5 year statutory exclusivity period predominantly overlaps with patent protection on the underlying biological product and is about 5-11 months shorter than the average remaining period of such patent protection on the original product.⁸

This seeming redundancy raises questions regarding the need for and purpose of having patents in inventions related to biologics *in addition* to statutory exclusivities. What justification

additional optional one year for approval of additional treatment indications for the same product. *See* Regulation (EC) No. 726/2004 of the European Parliament and of the Council, Art. 14(11) (2004). For further discussion of the European regulatory framework for the approval of generic biologics, *see generally* Liang, *supra* note 2, at 397-408; Kelly & David, *supra* note 3, at 122-123.

⁶ For purposes of the discussion in this Article, a "statutory exclusivity" is defined as the period of time designated in legislation during which the FDA or any other statutorily designated entity is barred from approving a generic version of a product or taking other action mandated in legislation which would pave the road for competition in that product. The effect of such statutory impediment is a de-facto grant of a competitive advantage to the party owning/making the original version of the product. *Cf.* Bruce S. Manheim et al., 'Follow-On Biologics': *Ensuring Continued Innovation In The Biotechnology Industry*, 25 Health Affairs 394, 394 (2006), available at <http://content.healthaffairs.org/cgi/content/full/25/2/394> (defining "statutory exclusivity" as "the period of time in which the FDA is barred from approving a follow-on product."). For further discussion of statutory exclusivities and the difference between them and intellectual property rights such as patents *see infra* Part II.A. Two examples of statutory exclusivities existing in the context of FDA regulation are those affected under the Drug Price Competition and Patent Term Restoration Act of 1984 and the Orphan Drug Act. *See* Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act), Pub. L. No. 98-417, 98 Stat. 1585 (Codified as amended in different sections of 15, 21, 35 and 42 U.S.C.); Orphan Drug Act, Pub. L. No. 97-414, 6 Stat. 2049 (1983). For further discussion of these Acts and the statutory exclusivities they confer *see infra* Part II.B.

⁷ Patient Protection and Affordable Care Act, Pub. L. No. 111-149, §§ 7001-7002, 124 Stat. 1025 (2010) (adding § 351(k)(7) to the Public Health Service Act (PHSA) ch. 373, 58 Stat. 682 (1944)). *See* discussion *infra* III.B. Importantly, in February 2011, as part of its 2012 Budget Proposal, the Office of Management and Budget in the Executive Office of the President published a proposal to shorten this exclusivity period to 7 years. *See* Office of Management and Budget, Fiscal Year 2012 Terminations, Reductions and Savings – Budget of the U.S. Government, at 119 ("[t]he Administration is proposing to give consumers more access to affordable pharmaceuticals by . . . reducing the exclusivity period for brand biologics to encourage faster development of generic biologics . . . Under the Administration proposal, beginning in 2012, innovator brand biologic manufacturers would have 7 years of exclusivity). Interestingly, this proposal appears to be in line with the Administration's original position on the appropriate length of statutory exclusivity that should be awarded in approved original biological products. *See infra* note 87. Regardless, the discussion herein is based on the law as it currently stands under BPCIA.

⁸ *See* discussion *infra* Parts IV.A-IV.B.

is there, if any, for such double-layered protection in biologics? And, assuming that such justification or need for double protection does exist, why should pharmaceutical biologics be the only kind of technology to benefit from it? Could the statutory exclusivity regime in pharmaceutical biologics mark the dawn of a new era in the protection and incentivizing of innovation and the beginning of a gradual replacement of the old patent system with modern schemes of statutory exclusivities; or is it just a peculiar case of a legal regime shaped by an unusually powerful industry? In this article I will seek to answer these questions.

Part II of this article will review fundamental patent theory concepts necessary for the discussion and compare them with statutory exclusivities with emphasis on the statutory exclusivity scheme created under the Hatch-Waxman Act. Part III will describe the current regulation of biologics in the United States and review the framework for the approval of generic biologics under BPCIA. Comparing statutory exclusivities and patent protection in the context of biologics, Part IV will discuss the “pros” and “cons” of these two regimes from a public policy perspective, address the possible ramifications of having both statutory exclusivities and patent protection in biologics and culminate in a call for the suspension of patent enforcement rights with relation to biological products that benefit from statutory exclusivities afforded under BPCIA for the duration of such exclusivities. Part V will include broader conclusions regarding additional areas of technology which could benefit from the application of statutory exclusivities regimes.

II. Statutory Exclusivities and Patents as Mechanisms of Protecting and Advancing Technological Innovation

A. Patents

Dating as far back as the 15th Century,⁹ patents¹⁰ are time-limited monopolies granting inventors the right to exclude others from using their patented inventions;¹¹ i.e., for a predefined period of time, inventor-patentees can dictate whether and how third parties may practice their patented inventions and collect payments in exchange for their permission to do so. The literature on patent theory is vast, but two theories dominate the underlying rationales for having patent systems.¹²

⁹ See Giulio Mandich, *Venetian Patents (1450-1550)*, 30 J. Pat. Off. Soc’y 166, 169 (1948).

¹⁰ In the context of this Article, unless stated otherwise, reference to “patents” is to the modern form of patents of invention—i.e. utility patents—as opposed to design patents, plant patents and other types of patents.

¹¹ In the United States, the right to exclude includes the making, using or selling of the invention or importation of the invention into the United States. See 35 U.S.C. § 271(a). See also Fritz Machlup, Subcomm. on Patents, Trademarks, and Copyrights, & Senate Comm. On the Judiciary, 85th Cong., 2d Sess., *An Economic Review of the Patent System* at 1 (Comm. Print 1958) (“a patent confers the right to secure the enforcement power of the state in excluding unauthorized persons for a specified number of years, from making commercial use of a clearly identified invention”).

¹² The exact rationales for having patents remain the subject of debate. Although it is generally accepted that inventive activity is responsive to economic stimuli, the need for patents as effective and efficient means of providing such stimuli remains under debate. See Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. Chi. L. Rev. 1017, 1031 (1989) (“[t]here is considerable empirical evidence suggesting that technological change has been an extremely important source of economic growth over time, and that levels of invention are responsive to economic stimuli. But it does not necessarily follow that patent protection is necessary to preserve adequate economic incentives for invention and innovation”). Notably, the patent theory literature recognizes additional rationales for patents. E.g. the proposition that patents are a natural right because inventors have natural property rights in their ideas and thus, to prevent theft of such ideas by unauthorized parties, society is morally obliged to afford inventors a proprietary right in their inventions that would confer exclusivity in the invention. See Machlup, *supra* note 11, at 21. Another somewhat archaic rationale for patents is the proposition that patents are means of securing appropriate rewards, namely, that principles of justice and “natural law” require that inventors receive rewards for their inventions proportional to the inventions’ usefulness to society. See Machlup, *supra* note 11, at 21.

1. Patents as Incentive to Disclose

According to this theory, patents embody a pact between inventors and society: in exchange for revealing their inventions to society and the way to utilize them, society grants inventors monopoly rights in their inventions for a limited period of time.¹³ This patent theory presumes that inventors would have kept their inventions a secret for as long as possible but the exclusivity is sufficient to convince them to disclose and explain their inventions and thus benefit society.¹⁴ An underlying premise of this theory is that the required disclosure of the invention by the inventor, once made, will enable the public to use the technology.¹⁵ These assumptions have been the subject of critique, especially in view of arguments that many patents withhold vital information necessary for utilizing the inventions without additional, sometimes substantial, research and development (R&D).¹⁶

2. Patents as Incentive to Invent/Invest

A modern, broadly accepted perception of patents is as an instrument of incentivizing invention by affording inventors an extra-competitive advantage over their competitors.¹⁷

¹³ See Machlup, *supra* note 11, at 21 (the “exchange-for-secrets” thesis); Eisenberg, *supra* note 12, at 1022, 1028-1030 (“[i]n exchange for these exclusive rights, the patent statute requires the inventor to disclose the invention in the patent application in terms sufficient to enable others who are ‘skilled in the art’ to make it”).

¹⁴ See Machlup, *supra* note 11, at 21; Eisenberg, *supra* note 12, at 1028-1030.

¹⁵ See Machlup, *supra* note 11, at 21.

¹⁶ See Machlup, *supra* note 11, at 32-33 (“[t]he point that patent monopolies are often granted in exchange for incomplete disclosure is made by several writers . . . the unpatented secret knowledge which is necessary to use a patent is colloquially called the know how and is generally regarded as property distinct from the patent to which it applies”); Sean B. Seymore, *The Teaching Function of Patents*, 85 Notre Dame L. Rev. 621, 626 (2010) (recognizing that one critique of patents is that they “seldom teach enough so that someone can actually go out and actually do the invention without some additional work”).

¹⁷ See Machlup, *supra* note 11, at 21 (the “monopoly-profit-incentive” thesis); Eisenberg, *supra* note 12, at 1024-1026 (“[t]he incentive to invent theory holds that too few inventions will be made in the absence of patent protection

Described as “the fundamental economic justification of patents,”¹⁸ the basic premise upon which this theory is based is that under competitive conditions the profit made by inventors would not be high enough to justify their investment and that in order to make the inventive activities worthwhile to inventors, society must ensure that they are able to exploit their inventions to an extent that would sufficiently compensate them for their investment of time, money and effort.¹⁹

Further evolution of the incentive-to-invent theory views patents as vital not only for the inventive activity itself but also for the industrial application of resulting inventions,²⁰

because inventions once made are easily appropriated by competitors of the original inventor who have not shared in the costs of invention.”). Notably, this perception of patents also seems to lie in the basis of the Constitutional authorization of Congress to grant patents for the purpose of promoting scientific progress. *See* U.S. Const. Art. I § 8 Cl. 8 ([Congress shall have Power t]o promote the Progress of Science and useful Arts, by securing for limited Times to . . . Inventors the exclusive Right to their . . . Discoveries”). An important critique of the perception of patents as incentive-to-invent argues that Man would create and invent regardless of any prospect of gain. *See* Machlup, *supra* note 11, at 34 (quoting Frank W. Taussig).

¹⁸ Machlup, *supra* note 11, at 32.

¹⁹ *Id.* at 32, 37, 39 (reviewing arguments made by several scholars, including A.T. Hadley and Joseph Schumpeter); Brill, *supra* note 5, at 6 (“[t]he purpose of the patent system is to ensure that the inventor of a patented product receives monopoly market conditions and can earn profit margins sufficient to induce the R&D costs associated with bringing the product to market.”).

²⁰ For purposes of the discussion herein, this hypothesis will be referred to as the “incentive-to-invest” theory. Notably, the invention/investment terminology used herein bears similarity to the distinction drawn by some scholars between “invention” and “innovation.” For example, Eisenberg refers to the incentive-to-invest offshoot of the incentive-to-invent rationale as a separate patent theory according to which patents are meant to promote “innovation,” namely investment in practical and commercial development of existing inventions. *See* Eisenberg, *supra* note 12, at 1024 note 29, 1037-1045. *See also* Robert P. Merges, *Commercial Success and Patent Standards: Economic Perspectives on Innovation*, 76 Cal. L. Rev. 803, 807 (1988) (“[a]n invention refers to the practical implementation of the inventor's idea. This often takes the form of a prototype or model. An invention, then, is more than a concept (it is usually a tangible thing), but less than the fully worked out product or process first offered for sale to customers. An innovation is the ‘debugged’ and functional version of the invention: the version first offered for sale.”).

namely for the incentivizing of financing of the steps necessary for putting an invention on the market.²¹

Despite extensive criticism of the incentive-to-disclose and incentive-to-invent/invest theories,²² they offer means for evaluating the utility of patents. Thus, in examining patents in the context of biologics, I will assume that these patent theories are valid and capable of explaining, at least to some extent, the need for patent protection for inventions in general, and biotechnological inventions in particular.

B. Statutory Exclusivities

The classic view on monopolies, whether patent or otherwise, is that they are generally harmful to society, but “a temporary monopoly granted to an inventor [is] a good way of rewarding his risk and expense.”²³ This maxim is equally applicable to both patents and other types of state-instituted monopolies, such as statutory exclusivities, as a way to incentivize and reward innovation.²⁴

²¹ See *id.* Eisenberg; Machlup, *supra* note 11, at 36 (“[f]inancing the work that leads to the making of an invention may be a relatively small venture compared with that of financing its introduction, because costly development work, experimentation in production and experimentation in marketing may be needed before the commercial exploitation of the invention can begin”). The incentive-to-invest theory is especially relevant to the medical products industry, in which the expense in the laboratory of identifying a promising drug or biologic is often not remotely as costly as putting it through clinical trials as required by the FDA.

²² See e.g. Machlup, *supra* note 11, at 22-25 (describing critiques of arguments in favor of patent protection); Eisenberg, *supra* note 12, at 1026-1030 (addressing the critiques on the incentive-to-disclose and incentive-to-invent theories); and 2008 CRS Report, *supra* note 1, at 18. It is not within the scope of this Article to go into the details of such critiques.

²³ See Machlup, *supra* note 11, at 19. But see Brill, *supra* note 5, at 11 (warning from the chilling effects of too-long monopoly periods and arguing that “excessive monopoly protection by the government creates windfalls to innovators, stifles competition and is costly to society.”).

²⁴ E.g., the *sui generis* rights under the Plant Variety Protection Act (PVPA), Pub. L. 91-577, 84 Stat. 1542 (1970) (codified as various sections in 7 U.S.C.) and the Semiconductor Chip Protection Act of 1984, Pub. L. No. 98-620, 98 Stat. 3347 (codified in 17 U.S.C. §§ 901 *et seq.*). Notably, the arguments in favor of granting statutory

As mentioned above, a statutory exclusivity is a time-limited monopoly in a product or products which is the result of a bar on the entry of competitors into the product's market.²⁵ The most significant example of statutory exclusivities is that of the exclusivity periods granted under the Hatch-Waxman Act.²⁶ Creating the regulatory pathway for the approval of generic versions of small-molecule drugs, the Hatch-Waxman Act provides for several types of statutory exclusivities. First, the Hatch-Waxman Act offers a five-year statutory exclusivity period available to original drug manufacturers for receiving marketing approval of drugs containing therapeutic chemical compounds that have not been previously approved for medical use.²⁷ As I will explain later in this article, although the five-year NCE exclusivity and 12-12.5 year statutory exclusivity under BPCIA may seem like they are meant to function in the same way—as though the 12-12.5 year market exclusivity is “NCE exclusivity for biologics”—their purpose

exclusivities in biologics—encouraging innovation and enabling innovators to gain sufficient profit—bear striking resemblance to the incentive-to-invent/invest patent rationale discussed above. *See infra* notes 72-73 and accompanying text. For further discussion of the resemblance between the rationales for granting patents and statutory exclusivities, *see infra* Parts IV.C.

²⁵ *See supra* note 6. In terms of their effect, statutory exclusivities are highly similar to patents. According to Machlup, patents have three characterizing features: conditionality, limitation of time and scope and their being awarded by society for a recognizable reason. Machlup, *supra* note 11, at 26 (“most writers [writing about patents] want to make it understood that [patents] are not “odious” monopolies but rather “social monopolies,” “general welfare monopolies,” or “socially earned” monopolies . . . [all patent monopolies] are “limited and conditional.””).

²⁶ *See* Hatch-Waxman Act, *supra* note 6. For an overview of the Hatch-Waxman Act and its legislative history *see generally* Gerald J. Mossinghoff, *Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*, 54 Food & Drug L.J. 187 (1999); Gitter, *supra* note 2, at 568-573.

²⁷ *See* 21 U.S.C. §§ 355(c)(3)(E)(ii). This exclusivity period is commonly known as ‘New Chemical Entity’ (NCE) exclusivity. During the NCE period of exclusivity, a generic version of the same drug cannot be approved. *Id.* However, a generic applicant may file an application for the approval of a generic version of the drug after four years by challenging the patents related to the original product under 21 U.S.C. § 355(j)(5)(B)(iv)(II). Such a challenge would normally prompt the filing of a lawsuit by the patent owner, which would trigger – regardless of the timing in which the challenge was made with relation to the NCE exclusivity – an additional period of 30 months (or 7.5 years from the date of approval, if the filing was made between NCE years 4-5) during which the FDA may not approve the generic application. *See* 21 U.S.C. § 355(j)(5)(B)(iii). For further discussion of the NCE exclusivity period and its underlying rationale *see infra* Part III.C.

is in fact quite different.²⁸ Additionally, the Hatch-Waxman Act creates a three-year statutory exclusivity period for conducting additional clinical investigations that lead to the approval of an additional new medical use of an already approved drug.²⁹ Finally, the Hatch-Waxman Act seeks to incentivize the creation of generic versions of drugs by granting a 180-day exclusivity period to companies that are first to file applications for the marketing of generic versions of an original drug product.³⁰ However, in order to receive the 180-day exclusivity, a generic applicant must challenge patents related to the original drug.³¹ The flourishing generic drug market and the entire generic drug industry are commonly viewed as attributable to this statutory exclusivity scheme created under the Hatch-Waxman Act.³²

Another important example of a statutory exclusivity framework is that of the exclusivities granted under the Orphan Drug Act³³ to developers of drugs for rare diseases³⁴ such

²⁸ See *infra* note 92 and accompanying discussion.

²⁹ See 21 U.S.C. §§ 355(c)(3)(E)(iii)-(iv). This additional exclusivity period is meant to incentivize further investment in R&D of a known drug.

³⁰ See 21 U.S.C. § 355(j)(5)(B)(iv). Notably, the benefit embodied in the 180-day exclusivity period for generic manufacturers lies in the recipient's ability to charge near-monopoly prices for its generic version of the drug for the duration of the 180-day exclusivity period. See Gitter, *supra* note 2, at 573 (noting that during the 180-day period the generic drug "shares duopoly prices with the Brand-name drug").

³¹ See 21 U.S.C. § 355(j)(5)(B)(iv)(II). Thus, the Hatch-Waxman Act itself incentivizes the challenging of patents related to the original drug product. In this respect, the Hatch-Waxman Act seeks to abolish one monopoly by offering another, shorter one.

³² The Hatch-Waxman Act is considered a great success in terms of incentivizing R&D activities and in monetary terms due to the savings attributable to the approval of generic versions of innovative drugs. See Gitter, *supra* note 2, at 586-587 (reviewing the reasons for what she describes as the "overall success" of the Hatch-Waxman Act); Liang, *supra* note 2, at 365 (arguing that the Hatch-Waxman Act has been very successful in bringing cheaper generic versions of drugs to the market while maintaining incentives for continued innovation).

³³ Orphan Drug Act, Pub.L. 97-414, 96 Stat. 2049 (1983) (codified as 42 U.S.C. § 360aa *et seq.*).

³⁴ See 21 U.S.C. §360bb(a)(2) (definition of "rare disease or condition"). Notably, the definition of an orphan drug could also include "orphan" biologics approved under PHSA § 351.

as Huntington’s disease, ALS (Lou Gehrig’s disease) and Tourette syndrome.³⁵ Under the Orphan Drug Act, once an approved drug or biologic is approved and “designated under [21 U.S.C §360bb] for a rare disease or condition, the [FDA] may not approve another application . . . for such drug for such disease or condition for a [generic applicant] until the expiration seven years from the date of the approval of the [drug or biologic].”³⁶ The idea behind the legislation of the Orphan Drug Act was to increase insufficient financial incentives under patent law (if any) by supplementing it with an additional exclusivity period that would make the development of drugs for rare diseases financially feasible.³⁷ The addition of the statutory exclusivity period that is the crux of the Orphan Drug Act is considered to have achieved its desired effect: since its passage in 1983, more than 200 drugs and biologics for rare diseases have been brought into the market as compared with fewer than ten in the decade preceding the passage of the Act.³⁸

C. Patents and Statutory Exclusivities—Similarities and Differences

The main difference between statutory exclusivities and patents involves the nature or type of “right.”³⁹ Patents result from a *grant* by an executive agency—the United States Patent and Trademark Office (USPTO)—and create a right to exclude others from using the object of

³⁵ See Congressional Findings for the Orphan Drug Act § 1.

³⁶ 21 U.S.C. § 360cc(a)(2).

³⁷ See Congressional Findings for the Orphan Drug Act, *supra* note 35, §§ 2, 4-5. Notably, such orphan drug products may be entirely unpatentable and could still merit exclusivity under the Orphan Drug Act.

³⁸ See FDA, *Developing Products for Rare Diseases & Conditions*, available at <http://www.fda.gov/forindustry/developingproductsforrareconditions/default.htm>; Frank R. Lichtenberg & Joel Waldfogel, *Does Misery Love Company? Evidence from Pharmaceutical Markets Before and After the Orphan Drug Act*, 15 Mich. Telecomm. & Tech. L. Rev. 335, 348 (2009) (arguing that the Orphan Drug Act “works”).

³⁹ This part of the discussion will utilize the terminology and distinctions proposed by Hohfeld. See Wesley Newcomb Hohfeld, *Some Fundamental Legal Concepts as Applied in Judicial Reasoning*, 23 Yale L. J. 16 (1913).

the right, namely the invention.⁴⁰ A patentee's right to exclude is correlated with the duty of third parties not to use the invention without the patentee's permission.⁴¹

Statutory exclusivities, on the other hand, are the result of *inaction* by an executive agency that effectuates a *de-facto* monopoly status with respect to a particular product. For example, the NCE exclusivity under the Hatch-Waxman Act is a result of the prohibition of the FDA granting marketing approvals for generic versions of the original drug for a period of five years from the date of approval of that drug, thereby effectuating a five-year exclusivity in that drug on its developer.⁴² In other words, the benefits of statutory exclusivities to developers of original products are by-products of the preclusion of potential competitors by an executive agency's withholding of its permission to partake in a regulated activity.⁴³

The difference in the nature of the right conferred by patents and statutory exclusivities dictates two additional important distinctions related to the enforceability of the respective rights and their susceptibility to legal challenges. From an enforceability perspective, while patents

⁴⁰ Notably, patents are commonly mistaken for a positive right to use an invention. The distinction between a right to use and a mere right to exclude others may be best illustrated where a patentee is unable to use their own invention but still has the right to exclude others from using it. For example, if A's invention cannot be used without B's patented technology, then A would be unable to use B's technology although it would certainly still be able to prevent C from using A's technology even if C has a license from B to use B's technology.

⁴¹ See Hohfeld, *supra* note 39, at 32 (quoting *Lake Shore & M. S. R. Co. v. Kurtz*, 10 Ind. App., 60, 37 N. E., 303, 304 (1894): "[a] duty or a legal obligation is that which one ought or ought not to do. 'Duty' and 'right' are correlative terms. When a right is invaded, a duty is violated").

⁴² See discussion of NCE exclusivities *supra* note 27 and accompanying text.

⁴³ I.e., the FDA does not owe an original drug manufacturer a five-year monopoly status for having a new chemical compound approved for medical use. Rather, the FDA is merely obliged to refrain, for a period of 5 years, from approving generic versions of the particular chemical compound for the drug's indicated medical use. Put in Hohfeldian terms, statutory exclusivities are the result of a privilege granted to applicant A to partake in certain commercial activities requiring a license from an executive agency E. Yet, the exclusivity itself is not the result of the privilege but rather of an *immunity* of A from having its monopoly status changed which correlates to a non-ability of third parties C to abolish this monopoly status of A by securing approval of their own generic products from agency E. See Hohfeld, *supra* note 39, at 55 (discussing the concepts of immunity and disability).

give grantees the right to preclude others from taking certain actions as they relate to the inventions claimed by such patents,⁴⁴ statutory exclusivities are merely immunities and confer no right *per se* (in the narrow Hohfeldian sense) on their bearer.⁴⁵ Accordingly, enforcement of patent rights necessitates actively seeking relief from a court and, typically, requires significant investment of resources. Statutory exclusivities, on the other hand, are “automatically enforced” by the regulatory bar that preempts the entry of potential competitors into the relevant market and, thus, require no enforcement action *per se* on the part of the parties benefiting from them.⁴⁶

Patents and statutory exclusivities also differ in their susceptibility to legal challenges. Patents, while presumed valid,⁴⁷ are subject to several different types of challenges, including reexamination,⁴⁸ defense arguments in patent infringement suits⁴⁹ and suits for a declaratory

⁴⁴ See *supra* notes 11 and 40 and accompanying text.

⁴⁵ It is possible to argue that from a legal standpoint the beneficiaries of statutory exclusivities could secure certain *legal* rights, e.g. if agency E, for some reason, goes ahead and approves an application of third party C prior to the expiration of the relevant statutory exclusivity period, applicant A may be entitled to recover damages from agency E the amount that A could have reasonably expected to gain from its monopoly status had agency E not approved C’s application. In this regard, it is important to distinguish between the *type* of right per Hohfeld and the *legal* right. See e.g. Hohfeld, *supra* note 39, at 43–44 (explaining that there are “innumerable cases in which the mental and physical facts . . . [are] confused with the legal relation which they create”).

⁴⁶ See Brill, *supra* note 5, at 6 (“[d]ata exclusivity is a definitive monopoly and a government grant, as it allows the innovator’s data to be protected without challenge”); Joyce Wing Yan Tam, *Biologics Revolution: The Intersection of Biotechnology, Patent Law, and Pharmaceutical Regulation*, 98 Geo. L.J. 535, 553 (2010) (“[m]arketing exclusivities are particularly powerful . . . This perfect monopoly protection is automatic and does not require the entity holding the market exclusivity to act—a sharp contrast to patent rights, which are *only* enforced when the patent holder prevails in a legal action.”). However, a party benefiting from a statutory exclusivity *could* attempt to preserve and possibly even extend its monopoly by filing a citizens petition requesting the FDA to take certain actions (e.g. imposing increased testing requirements on generic applicants) or refrain from taking certain actions (e.g. approving a generic application). See 21 C.F.R. § 10.30.

⁴⁷ See 35 U.S.C. § 282 (“[a] patent shall be presumed valid”).

⁴⁸ See 35 U.S.C. §§ 302–305.

⁴⁹ Patent infringement suits initiated under the Hatch-Waxman Act normally fall under this category. Namely, the third party generic applicant makes a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) that the patents covering the original drug product are “invalid or will not be infringed by the manufacture, use, or sale of the new drug for

judgment.⁵⁰ Such challenges could and often do result in the partial or complete invalidation of the challenged patents.⁵¹ Hence, it is possible to say that patents are substantially exposed to legal challenges throughout their term.

Statutory exclusivity status, however, can only be contested by challenging the relevant agency's inaction (i.e. omission), e.g., by disputing the agency's "failure" to approve an application to partake in the particular regulated activity which is the subject of the exclusivity. Since such a challenge would essentially argue that the agency should have, purportedly, approved the additional, later application, its prospects of success in court are not high from the outset.⁵² Thus, statutory exclusivities are substantially less susceptible to legal challenges than patents.

which the application is submitted." Under patent law, such certifications constitute acts of infringement under 35 U.S.C. § 271(e)(2). See discussion *supra* notes 30-31 and accompanying text.

⁵⁰ Suits for declaratory judgment may be brought under 28 U.S.C. § 2201, *but see* Federal Food, Drug, and Cosmetic Act (FFDCA) (Copeland Pure Food and Drugs Act) (Food, Drug, and Cosmetic Act) (FDCA) (Humphrey-Durham Act), ch. 675, 52 Stat. 1040, §§ 505, 512 (1938).

⁵¹ For example, patents are susceptible to challenges involving their novelty and non-obviousness under 35 U.S.C. §§ 102-103, their compliance with the various requirements of 35 U.S.C. § 112, their being directed to patentable subject matter under 35 U.S.C. § 101, and so forth.

⁵² Under current Supreme Court Precedent, challenging executive agencies' inaction is likely to be unsuccessful. See *Hackler v. Chaney*, 470 U.S. 821, 831 (1985) ("[t]his Court has recognized on several occasions over many years that an agency's decision not to prosecute or enforce, whether through civil or criminal process, is a decision generally committed to an agency's absolute discretion). This low likelihood of success of an attempt to challenge executive agencies' inaction is especially true in the context of drug law. See *Hackler v. Chaney*, 470 U.S. at 835-36 (rejecting the argument that the FFDCA's prohibitions of "misbranding" and the introduction of "new drugs" absent agency approval supply courts with "law to apply" and therefore do not provide a basis for judicial review of an FDA decision not to take enforcement action in the area of drug law). See also Brill, *supra* note 5, at 6 ("[d]ata exclusivity is not challengeable in court").

Although statutory exclusivities *per se* may be relatively unsusceptible to legal challenges, it is quite possible that an agency's interpretation and application of laws instituting such exclusivities would be subject to legal challenges. However, such challenges would be subject to an exacting review standard of the Chevron Doctrine. See *Chevron U.S.A. Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 842-44 (1984) (holding that "considerable weight should be accorded to an executive department's construction of a statutory scheme. . . ." and that so long as (1) "Congress has [not] directly spoken to the precise question at issue", and (2) "the agency's answer

Having laid down some of the foundations necessary for a discussion of patents and statutory exclusivities in the context of biologics, I will now provide background on the regulation of biological products.

III. The Regulation of Biologics in the United States

A. The Approval of Biologics License Applications Under PHSA § 351

In order to introduce a biological product (including biologics) into interstate commerce the product's developer must first receive a biologics license from the FDA.⁵³ Under FDA regulations, the FDA may grant a biologics license pursuant to the submission of a biologics license application (BLA) showing that the biological product is sufficiently safe, effective and pure.⁵⁴ Demonstrating compliance with the FDA's safety, efficacy and purity standards normally requires having the biological product undergo extensive and lengthy R&D and regulatory approval processes.⁵⁵ Naturally, these R&D and approval efforts impose significant financial burdens on BLA applicants and the price of putting a new biological product on the

is based on a permissible construction of the statute" then "the principle of deference to administrative interpretations [should be] followed."').

⁵³ Under PHSA § 351(a)(1)(A), "[n]o person shall introduce or deliver for introduction into interstate commerce any biological product unless . . . a biologics license is in effect for the biological product." Notably, the FDA has approved several biologics through regulatory pathways created by FFDCA, e.g. human insulin products such as Humulin® and Humalog®, human growth hormone products such as Humatrope®, Norditropin® and Saizen® and more. See Vernon *et al.*, *supra* note 4, at 59-60 (discussing approval of some biologics under the framework of FFDCA). These biologics have mostly been well known, less structurally-complex compounds and, in some cases, are versions of already-approved biologics that have gone off-patent. However, such cases are an exception to the general rule that biologics are subject to the approval processes set forth primarily in PHSA and it is likely that the formation of a regulatory pathway for the approval of generic biologics under BPCIA (*see infra* Part III.C) would marginalize them even further. Thus, in analyzing implications of BPCIA, I will assume that future regulation of biologics is going to be done almost primarily, if not exclusively, under PHSA.

⁵⁴ See PHSA § 351(a)(2)(B)(i)(I); 21 C.F.R. § 600.2 *et seq.*

⁵⁵ See e.g. 21 C.F.R. §§ 601.2(a), 601.20, 601.25, 601.27 and 601.70. For further discussion of the typical length of the development of biological products *see infra* Part IV.A.

market is commonly estimated at around \$1.24-1.32 billion on average for a typical product.⁵⁶ As a result, biologics are usually very expensive.⁵⁷

While the high prices of biologics may be justified, they also give rise to concerns of possible abuses of market position by manufacturers of original biologics. Some commentators have argued that manufacturers of original biological products use the high entry barriers into the biologics' market⁵⁸—the result of the significant time, money and expertise necessary in order to put biologics on the market—to charge very high prices for their products well after they have recouped their development costs.⁵⁹ One of the proposed solutions for this perceived market failure is the creation of a regulatory pathway for the approval of generic versions of biologics.⁶⁰

⁵⁶ See Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?* 28 Manage. Decis. Econ. 469, 475 (2007) (estimating the cost of putting a typical biologic on the market, including taking under account success in obtaining regulatory marketing approval, at around \$1.24-1.33 billion (2005 US\$)) [hereinafter DiMasi & Grabowski]; Gitter, *supra* note 2, at 567, 589 (reviewing the significant investment required from biologics' manufacturers as compared to small-molecule drugs); Katlikoff, *supra* note 5, at 8 ("bringing a new biologic medication to market is exceptionally expensive—an estimated \$1.24 billion."); Vernon *et al.*, *supra* note 4, at 66-68 (discussing the high costs involved in the development and manufacturing of biologics). Notably, these high development costs are at least partially attributable to the fact that only about one in three biological products that start clinical trials eventually receive FDA approval. See BIO White Paper, *supra* note 2, at 4 ("it is estimated that less than a third of the biopharmaceuticals that enter clinical trials ever receive marketing approval").

⁵⁷ The annual price of some biologics tends to be very high and some of them could even cost over \$100,000, and in rare instances even over \$300,000 a year. See Kathleen R. Kelleher, *FDA Approval of Generic Biologics: Finding a Regulatory Pathway*, 14 Mich. Telecom. & Tech. L. Rev. 245, 252 (2007) (discussing the reasons for the relatively high prices of biologics); Kendra Marr, *Biotech Campaigns for Easier Access to Generic Drug Market*, Wash. Post, Aug. 13, 2008 at D01 ("[t]reatment [with biologics] can cost a patient more than \$30,000 a year, prohibiting many from obtaining drugs"); FTC Report, *supra* note 5, at i ("annual treatment for breast cancer with . . . herceptin can cost \$48,000 and the annual treatment for rheumatoid arthritis with Remicade can cost approximately \$20,000"); Editorial, *When a Drug Costs \$300,000*, N.Y. Times, Mar. 23, 2008 at WK8, available at <http://www.nytimes.com/2008/03/23/opinion/23sun3.html> (discussing the high annual cost of some biologics used for treating rare diseases); Shapiro, *supra* note 4, at 4 (listing the high costs of several prominent biologics).

⁵⁸ See Gitter, *supra* note 2, at 589-590 (recognizing the high entry barriers faced by generic manufacturers seeking to enter the biologics market); Sarah Sorscher, *A Longer Monopoly for Biologics?: Considering the Implications of Data Exclusivity as a Tool for Innovation Policy*, 23 Harv. J.L. & Tech. 285, 304 (2009) (discussing the high entry barriers into the generic biologics market, especially as compared to the entry barriers faced by manufacturers of generic small-molecule drugs).

⁵⁹ See Dinh, *supra* note 3, at 79 ("[b]esides the expenses of R&D and clinical trials, the high cost of biologics results from monopoly pricing of brand-name biologics . . . after patent expiration because the regulatory approval process

B. Regulatory Pathways for the Approval of Generic Pharmaceuticals—Background

As demonstrated by the generic scheme created under the Hatch-Waxman Act, regulatory frameworks for the approval of generic pharmaceuticals are established on the premise that identical or highly similar compounds could be assumed to be equally or similarly safe and effective⁶¹ and therefore require relatively little, if any, additional clinical testing prior to approval.⁶² The sought-after result of such lowered testing requirements is that the development costs of later products would be lower and, as a result, so would their prices, thereby increasing their affordability and accessibility. In other words, regulatory frameworks for the approval of generic versions of pharmaceuticals seek to save the high development costs involved in putting a candidate compound through all the stages of drug development by simply ensuring its identity

delays the market entry of competing products.”); Kelleher, *supra* note 57, at 252-253 (arguing that biologics are unjustifiably expensive and that the lack of competition in biologics costs the U.S. economy billions of dollars annually).

⁶⁰ The institution of a regulatory pathway for the approval of generic versions of an already approved drug was the solution chosen for a similar problem in the context of small-molecule drugs. See Hatch-Waxman Act, *supra* note 6. The legislation of the Hatch-Waxman Act (and the creation of the generic pharmaceutical industry that followed) was the result of the growing awareness during the 1970s and early 1980s to a similar situation that existed with relation to small-molecule drugs. For additional possible solutions to the market failure existing in the area of biologics see Sorscher, *supra* note 58, at 301-302 (reviewing additional mechanisms for addressing the problem of diminished competition in the biologics market such as cost-sharing and prize funding that could potentially facilitate access to proprietary biological products’ clinical data and manufacturing know-how).

⁶¹ See Dawn Willow, *The Regulation of Biologic Medicine: Innovators’ Rights and Access to Healthcare*, 6 Chi.-Kent. J. Intell. Prop. 32 (2006) (“[t]he principle underlying [a determination that two compounds have the same safety and efficacy profiles] is that the greater the degree of similarity or identity between the two [compounds], the greater the confidence that their clinical performance will be similar or the same.”); BIO White Paper, *supra* note 2, at 10 (“[b]eing identical to the innovator product allows FDA to rely on the innovator’s safety and effectiveness data in determining that the generic version of the product will be safe and effective.”).

⁶² See FTC Report, *supra* note 5, at ii (“[d]uplication of safety and efficacy information is costly, an inefficient use of scarce resources, and, as the FDA has explained, raises ethical concerns associated with unnecessary human testing”); Woodcock Statement, *supra* note 1, at 6 (“[b]y establishing that the drug product described in the [generic application] is the same as the approved innovator drug product, the [applicant can rely on the Agency’s finding of safety and effectiveness for the approved drug. Therapeutic equivalents can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling.”).

to or interchangeability with the original product.⁶³ Such identity or interchangeability, in turn, is deduced based on comparison of the original product with the generic product.⁶⁴

However, regulatory pathways for the approval of pharmaceutical products also invite free-riding by generic manufacturers who do not participate in the substantial investment normally involved in the R&D of pharmaceutical products.⁶⁵ Thus, it is necessary to ensure that developers of original pharmaceuticals are able to recoup their investment and reap profits sufficient to incentivize them to continue their R&D efforts. Both the Hatch-Waxman Act and BPCIA rely (at least to some extent) on statutory exclusivities for this purpose.⁶⁶ These

⁶³ Notably, the ability to achieve such identity or comparability between the biological compounds in the original biologic and the ones in a later, generic version of the biologic, thereby allowing recognition of the generic version of the biologic as interchangeable with the original product, has been a point of significant scientific and legal disagreement. For further discussion of the issue of biosimilarity and bioequivalence of biological compounds *see* Gitter, *supra* note 2, at 590-609 (arguing that current scientific knowledge enables making determinations regarding comparability of two biologics sufficient to justify an abbreviated regulatory pathway for the approval of protein-based biological products and making the case for such regulation); 2008 CRS Report, *supra* note 1, at 7-9 and 22-23 (describing the scientific and legal dispute regarding comparability of biological products); Woodcock Statement, *supra* note 1, at 1, 4 and 7-12 (stating that there is general recognition that the idea of “sameness” is not applicable to biologics in the same manner it is to small molecule drugs, addressing the FDA’s definitions for the terms “comparability,” “therapeutic equivalents” and “interchangeability” and reviewing the scientific challenges involved in comparing proteins and approving two biologics as substitutable/interchangeable); Liang, *supra* note 2, at 370-78, 415-17 (reviewing the difficulties in replicating biological compounds and the resulting safety concerns arising in the context of generic biologics); Marr, *supra* note 57 (describing the debate surrounding the ability to achieve and show similarity in biologics); Dinh, *supra* note 3, at 90-94 and 114-15. Notably, the enactment of BPCIA seems to accept the premise that there is, perceivably, a way to achieve and ascertain identity or similarity between two biological compounds.

⁶⁴ The comparison is of both the structures of the respective compounds and their physiological effects. *See* Willow, *supra* note 61 (“[b]y establishing that the drug product described in the [generic application] is the bioequivalent of the innovator drug product approved [by the FDA], the [generic] applicant can rely on the FDA’s finding of safety and effectiveness previously determined for its counterpart brand drug.”). Notably, the generic applicant does not and is not expected to acquire the actual clinical safety and efficacy data for the original product, which—while submitted to the FDA as part of the approval process of the original product—is considered proprietary, but rather “refers” the FDA to such data already in the FDA’s possession. *See* discussion *infra* note 160 ¶2.

⁶⁵ *See* 2008 CRS Report, *supra* note 1, at 20-21 (demonstrating the differences in cost and risk between development of an original new pharmaceutical and a generic version thereof).

⁶⁶ *See*, respectively, *supra* Part II.B and *infra* Part III.C. I will argue later in this article that the statutory exclusivities afforded to developers of original pharmaceuticals under the Hatch-Waxman Act are different from the ones instituted under BPCIA not only in their length – 3-6 years as compared to 12-12.5 years respectively – but

exclusivities, despite differences in their length and scope, all essentially guarantee that for a certain amount of time the government will not allow potential competitors to enter the relevant market or take steps toward doing so.⁶⁷

C. The Framework for the Approval of Generic Biologics Under the Biologics Price Competition and Innovation Act

With the increase in the prevalence of biologics,⁶⁸ there have been increasing calls and proposals for the institution of a framework for the approval of generic versions of biologics.⁶⁹

also in their purpose and in the extent of protection that they afford to the interests of developers of original pharmaceutical products. See discussion *infra* Part III.C.

⁶⁷ It is common to refer to two main types of exclusivities in the context of regulatory frameworks for approval of generic pharmaceuticals products: (1) “market exclusivity” (also sometimes referred to as “approval exclusivity”): a period during which potential competitors are not allowed to enter the particular product’s market, which is typically enforced by a prohibition on the FDA to approve applications for comparable products for the duration of the exclusivity period. (Notably, market exclusivity granted to a generic product is sometimes referred to as “generic exclusivity.”); and (2) “data exclusivity,” which is a period of time during which potential competitors may not rely on FDA findings of safety and efficacy of an earlier approved product necessary to support the generic application, which is typically enforced by a prohibition on submission of generic applications for the duration of the exclusivity period. See Mossinghoff, *supra* note 26, at 189 (explaining that a period of exclusivity during which a generic version of a drug cannot be approved is generally referred to as “data exclusivity”); Gitter, *supra* note 2, n. 113 (defining “market exclusivity” and “generic exclusivity”); Kotlikoff, *supra* note 5, at 3, 5 (explaining what data and market exclusivities are). Notably, the terms “market exclusivity” and “data exclusivity” have been defined rather loosely in the literature and sometimes have different meanings. See e.g. Gitter, *supra* note 2, n. 108 (referring to “data exclusivity” as the period during which the FDA cannot approve an ANDA for a generic drug). The Hatch-Waxman Act establishes three market exclusivity periods (five years for NCE, three years for approval of a known drug for a new indication and 180 days for approval of a generic version further to challenging the patents related to the original drug) and a data exclusivity period of four to five years. See 21 U.S.C. §§ 355(j)(5)(F)(ii)-(iv).

⁶⁸ See *supra* note 4.

⁶⁹ See *supra* note 3. Some prominent proposals for the institution of a regulatory pathway for approval of generic versions of biologics include H.R. 1038, 110th Cong., Access to Life-Saving Medicine Act (introduced Feb. 14, 2007) (‘ALSMA’); H.R. 1956, 110th Cong., Patient Protection and Innovation Biologic Medicines Act of 2007 (introduced Apr. 19, 2007) (‘PPIBMA’); S. 1695, 110th Cong., Biologics Price Competition and Innovation Act of 2007 (introduced June 26, 2007) (‘BPCIA 2007’); H.R. 5629, 110th Cong., Pathway for Biosimilars Act (introduced March 13, 2008) (‘PFBA’); H.R. 1427, 111th Cong., Promoting Innovation and Access to Life-Saving Medicine Act (introduced March 11, 2009) (‘PIALSMA’); H.R. 3590, 111th Cong., Biologics Price Competition and Innovation Act of 2009 §§ 7001-7002 (introduced Sep. 17, 2009) (‘BPCIA’); (introduced Sep. 17, 2009) (‘PPACA’) (the Senate vehicle for healthcare reform legislation; passed Senate by a Yay-Nay vote 60-39 on December 24, 2009); H.R. 3962, 111th Cong., Affordable Health Care for America Act §§ 2575-2577 (introduced Oct. 29, 2009) (‘AHCAA’) (highly similar to BPCIA). See also PBA, *supra* note 7.

As could be expected, some of these proposals were more favorable to generic manufacturers while others better represented the interests of developers of original biological products.⁷⁰ Yet, almost all of the proposals mandated the institution of some statutory exclusivity periods in original biologics, and especially a market exclusivity period of 12-15 years.⁷¹

The reoccurrence of a twelve-year period in many of the proposals has not been coincidental. Rather, it was the result of a perception that “the effective patent life for pharmaceuticals—the time remaining following FDA approval—is approximately eleven to twelve years.”⁷² Thus, an exclusivity period of about 12 years would presumably provide developers of original biologics with the assurance that the return on their investment would justify the time, money, and effort they expended in developing their products.⁷³ Notably, this

⁷⁰ E.g. ALSMA and PIALSMA were considered more “pro-generic” as they generally set more lenient comparability standards, shorter exclusivity periods for original products and better incentives for potential competitors to enter the market than “pro-innovators” bills such as PPIBMA and PBA, which set stringent comparability standards and long exclusivity periods for developers of original biological products. *See* ALSMA, relevant sections to be added as PHSA §§ 351(k)(4) and (10); PPIBMA, relevant sections to be added as PHSA §§ 351(k)(2)(D) and (3)-(6); PIALSMA, relevant sections to be added as PHSA §§ 351(k)(1)-(3), (5)(B) and (8)-(11); and PBA, relevant sections to be added as PHSA §§ 351(k)(2), (4), (6)-(7) and (9).

⁷¹ Under PPIBMA, developers of original biologics would have received exclusivity periods of 12-15 years; under BPCIA 2007, BPCIA and AHCAA, 12-12.5 years; under PFBA and PBA, 12-14.5 years; and under PIALSMA, up to six years. The exception was ALSMA that did not provide for exclusivity to developers of original biologics.

The length of exclusivity periods to be afforded to original biologics also was the subject of a heated debate regarding the optimum period of delay of generic entry into the market. *See* Gitter, *supra* note 2, 613-616 (reviewing some of the proposals for exclusivity periods in original biological products). While it is beyond the scope of this Article to assess what is the “optimum period” of monopoly in the context of biologics, notably, according to Machlup, “there will always be the possibility of very expensive developments that cannot be profitable even if a 30- or 50-year monopoly grant were promised.” *See* Machlup, *supra* note 11, at 39.

⁷² *See* FTC Report, *supra* note 5, at vi (“[t]he economic model put forth by pioneer drug manufacturers to justify [a 12-14-year exclusivity period] is based on the average time required to recoup the investment to develop and commercialize a typical biologic drug”); Grabowski 2009, *supra* note 5, at 4 (“[t]he average market exclusivity period for small molecule drugs in the United States is approximately twelve years.”); Gitter, *supra* note 2, at 616. *But see* Brill, *supra* note 5; Kotlikoff, *supra* note 5.

⁷³ *See* Kelleher, *supra* note 57, at 256 (“[b]iologics cost more to produce than [small-molecule] drugs, and thus a five-year market exclusivity similar to the Hatch-Waxman provision may not be long enough to incentivize the

need for assurance in the case of biologics reflects an underlying assumption that patents alone cannot provide sufficient protection to the interests of developers of biological products.⁷⁴

Eventually, after years of debate, on March 21, 2010, Congress enacted BPCIA as part of the Obama Administration's healthcare reform⁷⁵ and on March 23, 2010, President Obama signed the act into law.⁷⁶ Originally introduced on September 17, 2009 as part of the Senate's healthcare reform bill, BPCIA is the reintroduction of BPCIA 2007.⁷⁷ BPCIA amends PHSA § 351,⁷⁸ the FFDCA and patent law creating a regulatory pathway for the licensing of biological products as “biosimilar to”⁷⁹ and/or “interchangeable with”⁸⁰ an already approved biological

development of biologics . . . some have suggested that a twelve-year market exclusivity for pioneer biologics would be optimal because traditional drugs generally have slightly under 12 years of market exclusivity due to patent protection”); Kelly & David, *supra* note 3, at 139-140 (“[a] 12 to 14 year period of innovator exclusivity is not arbitrary: studies have shown that the point at which an innovator biological drug becomes profitable (the ‘break-even’ point) is between 12.9 and 16.2 years.”).

⁷⁴ See Kelleher, *supra* note 57, at 256 (reviewing the flaws of patent protection for biological products and arguing that “while traditional new [small-molecule] drugs are generally protected by patents, biologics may be less effectively protected by the patent system”). As I will argue later in this Article, for these same reasons (as well as others) patent protection for the underlying inventions related to biological products should be foregone during the period of statutory exclusivity under BPCIA. See *infra* Part IV.C.1.

⁷⁵ Patient Protection and Affordable Care Act §§ 7001-7003 (2010).

⁷⁶ See Sheryl Gal Stolberg and Robert Pear, *Obama Signs Health Care Overhaul Bill, With a Flourish*, N.Y. Times, March 23, 2010, available at <http://www.nytimes.com/2010/03/24/health/policy/24health.html>. Notably, as discussed earlier, less than one year later, in February 2011, the same administration seems to have backed out of its earlier endorsement of BPCIA's twelve-year exclusivity period and is currently trying to limit this exclusivity period to seven years. See *supra* note 7.

⁷⁷ BPCIA is almost identical to BPCIA 2007 introduced two years earlier by the late Senator Ted Kennedy and cosponsored by Senator Orrin Hatch and former Senator Hillary Rodham Clinton. See Library of Congress website, available at <http://thomas.loc.gov/cgi-bin/thomas> (‘Thomas’).

⁷⁸ Codified at 42 U.S.C. § 262.

⁷⁹ Under BPCIA, term ‘biosimilar’ or ‘biosimilarity’ means that “the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components” and that “there are no clinically meaningful differences between the biological product and the [original] product in terms of the safety, purity, and potency of the product.” See BPCIA § 7002(b) (codified at 42 U.S.C. § 262(i)(2)).

product (“reference product”⁸¹).⁸² Once a biological product is deemed “interchangeable with” a reference product, under BPCIA it may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.⁸³

BPCIA sets a twelve-year market exclusivity period in original biologics⁸⁴ and a four-year data exclusivity period for the data submitted in support of the application for the original biologic.⁸⁵ BPCIA also provides for a possible extension of the twelve-year market exclusivity

⁸⁰ Under BPCIA, the term ‘interchangeable’ or ‘interchangeability’ means that “the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.” See BPCIA § 7002(b) (codified at 42 U.S.C. § 262(i)(3)).

⁸¹ Under BPCIA, the term ‘reference product’ means the single biological product licensed under PHSA § 351(a) (*see supra* Part III.A) against which a generic biological product is evaluated in an application submitted under BPCIA. See BPCIA § 7002(b) (codified at 42 U.S.C. § 262(i)(4)).

⁸² BPCIA § 7002(a) (codified at 42 U.S.C. § 262). BPCIA sets up numerous elaborate conditions and requirements for the establishment of biosimilarity to and/or interchangeability with a reference product. See *id.* (codified at 42 U.S.C. §§ 262(k)(2)-(4)).

⁸³ See *supra* note 80. A determination of interchangeability is the essence of generic legislation and the prize sought after by generic applicants. Once made, the interchangeability determination facilitates the “interjection” of the generic biological product into the existing market for the original product and enables it to benefit from the reference product’s client base.

⁸⁴ BPCIA § 7002(a) (codified at 42 U.S.C. § 262(k)(7)(A)).

⁸⁵ *Id.* (codified at 42 U.S.C. § 262(k)(7)(B)). Under BPCIA, during this period, generic applicants may not submit applications for the approval of their versions of biologics biosimilar to original biological products. For further discussion of data exclusivity, see *supra* note 67.

This interpretation of the BPCIA sections relating to the exclusivities grant has been contested and argued to be mistaken by a group of members of the House of Representatives who are identified as proponents in Congress of the brand-name pharmaceutical companies. See Letter from Reps. Anna Eshoo, Jay Inslee and Joe Barton to the Food and Drug Administration dated Dec. 21, 2010 (“Eshoo letter”). The stance advanced in the Eshoo letter is that BPCIA “does not provide ‘market exclusivity’ for innovator products. Rather, it provides data exclusivity for 12 years from the date of FDA approval.” *Id.* The Eshoo letter does not directly explain what the difference between the 12 and 4 year exclusivities established under BPCIA is but indirectly comments that “[BPCIA] does not prohibit or prevent another manufacturer from developing its own data to justify FDA approval of a similar of [*sic*] competitive product.” *Id.* The positions taken in the Eshoo letter have been criticized as opposed to good public policy as well as to the simple language of BPCIA. See *e.g.* Letter from Senators Sherrod Brown, John McCain, Charles Schumer and Tom Harkin to Dr. Margaret Hamburg, Commissioner of the FDA, dated January 24, 2011. Notably, as a post-enactment statement, the FDA is not obliged to give the positions expressed in the Eshoo letter substantial weight in its construction of the statutory language of BPCIA. See *Massachusetts v. EPA*, 549 U.S. 497, 530 n.27 (2007) (endorsing the position that “post-enactment legislative history is not only oxymoronic but

and four-year data exclusivity by an additional six-month period for having the biological product tested and approved for use in pediatric populations.⁸⁶ Thus, BPCIA creates market exclusivity periods in original biological products of up to 12.5 years and data exclusivity periods of up to 4.5 years.⁸⁷ Importantly, the statutory exclusivities established under BPCIA *do not* guarantee exclusivity to an original developer of a biological product where another, different (later) developer may seek approval for its own version of the same biological compound for the same medical condition by conducting its own clinical trials; independently taking its product through the FDA approval processes irrespective of and without seeking to rely on the approval of the earlier “original” biological product.⁸⁸

In addition, BPCIA establishes market exclusivity periods of 12-42 months for a manufacturer of a first biological product approved as interchangeable with the reference product.⁸⁹

inherently entitled to little weight”). Moreover, even if one is to ignore the non-conformity between the construction suggested in the Eshoo letter and the language of BPCIA itself, the Eshoo letter’s statutory construction fails to explain the difference between the 12 and 4 year statutory exclusivities. In other words, if the twelve-year statutory exclusivity is in fact data exclusivity, it appears to render the four-year statutory exclusivity established by the following subsection of BPCIA redundant. Accordingly, for at least this reason it is unlikely that the FDA would adopt the statutory exclusivity proposed in the Eshoo letter.

⁸⁶ BPCIA § 7002(g) (codified at 42 U.S.C. § 262(m)).

⁸⁷ Notably, the passage of BPCIA with its 12-12.5-year market exclusivity and 4-4.5-year data exclusivity periods is at odds with the Obama Administration’s outspoken opposition to such exclusivity periods, which it perceived as too long. *See* Letter from Nancy-Ann DeParle, Director, Office of Health Reform and Peter Orszag, Director, Office of Management and Budget to Representative Henry A. Waxman (June 24, 2009), *available at* http://energycommerce.house.gov/Press_111/20090625/biologicsresponse.pdf (expressing the Obama Administration’s position that an exclusivity period for original biological products of seven years “strikes the appropriate balance between innovation and competition”).

⁸⁸ This scenario may come to be where the market for the biological product is large enough to financially justify taking the product through another, separate regulatory approval by the FDA rather than wait for the lapse of the applicable BPCIA statutory exclusivity periods.

⁸⁹ BPCIA § 7002(a) (codified at 42 U.S.C. § 262(k)(6)). The determination of a market exclusivity period that would be afforded to a generic manufacturer depends on several factors, including whether a patent infringement

Importantly, while the underlying rationales for market exclusivity under BPCIA and the 5-year NCE statutory exclusivity under the Hatch-Waxman Act (on which the BPCIA market exclusivity is modeled) are similar, their function/“mechanism of action” is different. In both cases, the intention was to provide developers of pharmaceutical products with sufficient incentives to invest in R&D.⁹⁰ However, while the 5-year NCE statutory exclusivity was meant to work its effect *where no incentives existed from a patent perspective* (e.g. where the drug product contains a well known active compound that is not patentable),⁹¹ the 12-12.5-year market exclusivity under BPCIA appears to have been devised as a “fallback” option to patents, namely, as “insurance” in case they fail.⁹²

BPCIA also creates an intricate dispute resolution scheme for patent disputes arising in relation to the submission of applications for approval of biological products as biosimilar to or

lawsuit was filed subsequent to the filing of the generic application for the approval of the biological product at bar and its outcome and the marketing status of such product. *Id.*

⁹⁰ For the idea behind the NCE exclusivity established under the Hatch-Waxman Act, *see* Allan M. Fox and Alan R. Bennett, *The Legislative History of the Drug Price Competition and Patent Term Restoration Act of 1984* at 60 (1987) (“[t]he original Waxman Committee version . . . would have allowed granting four years of market exclusivity only to new chemical entities that for technical or scientific reasons are unpatentable”) and Remarks of Rep. Waxman, House Floor Debate, Cong. Rec. of Sep. 6, 1984, at H9113-H9114 (“the amendment provides a 5-year period of exclusive market life for drugs approved for the first time after enactment of the legislation. This provision will give the drug industry the incentives needed to develop new chemical entities whose therapeutic usefulness is discovered late when little or no patent life remains.”). For the idea behind the market exclusivity established under BPCIA *see supra* notes 72-73 and accompanying text.

⁹¹ *See id.* Fox and Bennett.

⁹² Notably, proponents of long market exclusivity periods in biological products have described such exclusivity as an “insurance policy” in case patents would fail. *See infra* note 144 and accompanying text. In other words, rather than provide protection in addition to patents or in case patents cannot be obtained, market exclusivity under BPCIA is meant to provide an “iron-clad, litigation-proof” protection of the interests of developers of biological products in case their patents fall short.

An interesting question, which exceeds the scope of this article, is whether statutory exclusivities could be classified as proprietary rights—possibly a new kind of property—and what would be the implications of such classifications.

interchangeable with a reference product.⁹³ Under BPCIA, within twenty days after acceptance of an application for a generic biologic by the FDA, the generic applicant is required to provide legal representatives of the reference product sponsor and other potential adversaries, under a duty of confidentiality, a copy of the application and additional information regarding the process used to manufacture the biological product.⁹⁴ Within sixty days after receipt of the information from the generic applicant, the reference product sponsor is required to (1) provide the generic applicant with a list of all patents for which the reference product sponsor believes a claim of patent infringement could reasonably be asserted against the generic applicant if it engaged in the making, using, offering to sell, selling or importation of the generic biological product, and (2) identify which of these patents it would be prepared to license to the generic applicant.⁹⁵ BPCIA then stipulates that within sixty days of receipt of the reference product sponsor's patent list, the generic applicant may (but does not have to) provide its own "counter-list" of patents with respect to which it believes a claim of patent infringement could reasonably be asserted by the reference product sponsor.⁹⁶ For each patent on the reference product sponsor's list and the generic applicant's counter-list, the generic applicant is required to provide either a "a detailed statement that describes, on a claim-by-claim basis, the factual and legal basis of the opinion of the [generic] applicant that such patent is invalid, unenforceable, or will not be infringed by the commercial marketing of the biological product" or a statement that it does not

⁹³ *Id.* (codified at 42 U.S.C. § 262(l)).

⁹⁴ *Id.* (codified at 42 U.S.C. § 262(l)(1)-(2)).

⁹⁵ *Id.* (codified at 42 U.S.C. § 262(l)(3)(A)). Notably, BPCIA stipulates that a reference product sponsor would be unable to sue for infringement of patents which it did not include on its list. *Id.* (codified at 35 U.S.C. § 271(e)(6)).

⁹⁶ *Id.* (codified at 42 U.S.C. § 262(l)(3)(B)).

intend to begin commercial marketing before the date of patent expiry.⁹⁷ Within sixty days of receipt of the generic applicant's detailed statement, the reference product sponsor is required, in turn, to provide a "counter-detailed statement" explaining, for each patent claim addressed in the generic applicant's detailed statement, "the factual and legal basis of the opinion of the reference product sponsor that such patent will be infringed by the commercial marketing of the biological product" as well as a response to the generic applicant's statements of invalidity and unenforceability.⁹⁸ Upon completion of the above exchanges of information and legal positions, BPCIA mandates that the parties must enter pre-litigation negotiations in order to decide, within fifteen days, which patents, if any, will be the subject of an infringement action.⁹⁹

Further, BPCIA addresses different litigation scenarios. First, BPCIA stipulates that within thirty days of the exchange of patent lists between the reference product sponsor and generic applicant or of the date of reaching an agreement on patents that would be the subject of an infringement action, the reference product sponsor is required to bring a patent infringement action with respect to the patents under dispute.¹⁰⁰ Second, at least 180 days prior to a first commercial marketing of a generic biological product, BPCIA requires the generic applicant about to launch the product to provide notice of the planned launch to the reference product sponsor, which may then seek to enjoin the generic applicant from moving ahead with the

⁹⁷ *Id.* (codified at 42 U.S.C. § 262(l)(3)(B)).

⁹⁸ *Id.* (codified at 42 U.S.C. § 262(l)(3)(C)).

⁹⁹ *Id.* (codified at 42 U.S.C. § 262(l)(4)-(5) and (7)). If the parties fail to reach an agreement, BPCIA sets up an elaborate mechanism to decide on the number and identity of such patents that would be the subject of such an infringement action. *See id.* (codified at 42 U.S.C. § 262(l)(5)).

¹⁰⁰ *Id.* (codified at 42 U.S.C. § 262(l)(6)). Notably, under BPCIA, if the reference product sponsor fails to assert certain patents after that timeframe, then a reasonable royalty is the sole and exclusive remedy that a court may grant it if it finds that such patents were infringed. *See id.* (codified at 35 U.S.C. § 271(e)(6)).

launch.¹⁰¹ Under BPCIA, such an injunction would hold until a court decision on pending issues of patent validity, infringement and enforceability arising with relation to patents included on any patent list previously exchanged by the parties under BPCIA.¹⁰² And third, BPCIA addresses declaratory judgment actions and mandates that if the generic applicant sent the reference product sponsor a copy of the generic product application as required, then declaratory judgment actions would be available to the parties only once the 180-day notice of commercial marketing is provided to the reference product sponsor.¹⁰³ However, the reference product sponsor may bring such actions even earlier if the generic applicant fails to comply with other requirements set by BPCIA.¹⁰⁴

The next part of this article will compare the current legal regimes under patent law and BPCIA as they pertain to biological products and examine the question of whether there is actually a need and justification for both types of protection in the context of biologics.

IV. Patents vs. Statutory Exclusivities in Biological Products—Timeline, Public Policy and the Interests of Biologic License Holders

A. Patent vs. Statutory Exclusivities in Biologics: A Timeline

The R&D and approval of biologics, from the first synthesizing of the biologic or a closely related compound through the approval of the BLA by the FDA,¹⁰⁵ is a long process

¹⁰¹ *Id.* (codified at 42 U.S.C. § 262(l)(8)).

¹⁰² *Id.* (codified at 42 U.S.C. § 262(l)(8)(B)).

¹⁰³ *Id.* (codified at 42 U.S.C. § 262(l)(9)).

¹⁰⁴ *Id.* (codified at 42 U.S.C. § 262(l)(9)(B)-(C)).

¹⁰⁵ Notably, one may also view the development of drugs and biologics as an ongoing process that includes further R&D subsequent to marketing approval by the FDA. See <http://clinicaltrials.gov/ct2/info/glossary#phaselv>

which typically spans over a period of over a decade.¹⁰⁶ Although all development projects are different, a rough estimate of a typical timeline for the development of a biological product consists of about 4-5 years of preclinical studies,¹⁰⁷ 6-9 years dedicated to clinical trials prior to the submission of a BLA¹⁰⁸ and another 12-16 months for the FDA to process and decide on the BLA.¹⁰⁹ In sum, the development of a biological product typically takes 11-15.5 years.¹¹⁰

(defining phase IV clinical studies as “[p]ost-marketing studies to delineate additional information including the drug’s risks, benefits, and optimal use.”).

¹⁰⁶ Grabowski 2008, *supra* note 5, at 481 (illustrating the length of the development process of biologics with the example of the anti-cancer biologic Avastin, whose active compound, bevacizumab, took about 15 years to develop and have approved by the FDA); Vernon *et al.*, *supra* note 4, at 68 (“[b]ringing a single new product to market requires huge sums of investor capital and often takes well over a decade). See also *infra* Part IV.B (discussing my finding that the average number of days between the filing of the first patent application pertaining to a biological product, which is indicative of R&D activities, and FDA approval of the product as pertaining to the seventy-nine biological products listed in Appendix A is 3728 days, i.e. about 10.2 years).

¹⁰⁷ See Dennis S. Fernandez et al., *The Interface of Patents with the Regulatory Drug Approval Process and How Resulting Interplay Can Affect Market Entry*, in *ipHandbook of Best Practices* 965, 966 (Krattiger et al. eds., 2007) (“[p]reclinical studies take an average of five years”); Grabowski 2008, *supra* note 5, at 486 (stating that preclinical R&D requires 4-5 years to produce several lead candidates); DiMasi & Grabowski, *supra* note 56, at 475, Table 3 (estimating that the time spent on preclinical studies of candidate biological products is about 52 months). “Preclinical studies” are the earliest phase in drug development beginning right after the identification of a candidate-compound and concluding with the filing of an investigational new drug application (IND) with the FDA. This step normally includes in-vitro and animal testing of the tested compound, pharmacodynamic studies and more. See Fernandez et al. at 966 (describing the discovery phase and preclinical studies of new drugs). Once an IND is submitted, unless the FDA places a hold on the IND, the applicant may begin clinical trials after thirty days. See 21 C.F.R. §§ 312.40(b)(1), 312.42. About 85% of all drugs for which an IND is filed are eventually approved for testing in clinical trials. See Fernandez et al. at 966.

¹⁰⁸ The clinical trials stage of development is typically divided into three phases preceding the submission of a BLA. Phase I involves testing the candidate compound on humans for the first time for safety, determination of a dosage range and identification of potential side effects and includes about 20-80 healthy individuals; Phase II involves testing the drug/biologic on about 100-300 volunteers having the condition that the drug/biologic is meant to treat to determine if it is effective and to further evaluate its safety; Phase III for different drugs/biologics varies greatly but normally involves 1000-3000 patients and is meant to confirm the drug/biologic’s effectiveness, monitor side effects, compare the drug to commonly used treatments, and collect information that will allow the drug/biologic to be used safely. See National Institutes of Health, *Understanding Clinical Trials*, <http://clinicaltrials.gov/ct2/info/understand#Q18>; telephone interview with FDA, CBER representative, Feb. 23, 2010 (on file with author) [hereinafter CBER interview]; 21 C.F.R. § 312.21. Notably, estimates of the length of the different phases of clinical trials vary among different commentators. According to Fernandez et al. Phase I could take, on average, from 1-3 years, Phase II: 2 years and Phase III: 3-4 years. See *id.* Fernandez et al. at 966. According to an unofficial estimate by a CBER staff-member, Phase I takes about one year on average, Phase II about two and Phase III, while varying greatly and depending on the amount to testing done by the applicant, normally takes, on average, about 3 years. See *id.* CBER Interview. Grabowski and DiMasi estimate that clinical

Based on the abovementioned timeframes and in view of the fact that statutory exclusivities in biologics only “kick in” upon FDA approval, BPCIA dictates that (1) manufacturers of generic versions of biologics would only be able to file applications for generic versions of biologics after 15-20 years from the inception of development of the original biological product,¹¹¹ and (2) the FDA may only approve such applications after 23-28 years from the inception of development of the original biologic.¹¹²

Viewing the abovementioned timeframes from a patent perspective, it is important to acknowledge several additional milestones. First, biologics may be and often are the subject of numerous patents that typically cover (1) specific biological compounds, namely the purified active biological compounds themselves (most frequently, proteins), their precursors, possible metabolites and other derivatives,¹¹³ (2) processes of making these compounds,¹¹⁴ (3)

trials take an average of about 6.8 years. See DiMasi & Grabowski, *supra* note 56, at 473, Figure 2 (estimating the time spent on clinical development of biologics at about 82 months).

¹⁰⁹ See *id.* CBER interview; DiMasi & Grabowski, *supra* note 56, at 473, Figure 2 (estimating the time spent on approval of biologics at about 16 months).

¹¹⁰ This calculation is based on adding the estimated 4-5 years of preclinical studies, 6-9 years of clinical trials and 1-1.33 years it takes the FDA to approve BLAs and then rounding the result (11-15.33 years) to the closest half-year increment.

¹¹¹ This calculation is based on adding the estimated 11-15.5 years it takes to put a typical biologic on the market to the 4-4.5 years of data exclusivity under BPCIA.

¹¹² This calculation is based on adding the estimated 11-15.5 years it takes to put a biologic on the market to the 12-12.5 years of market exclusivity under BPCIA.

¹¹³ See *Parke-Davis & Co. v. H.K. Mulford & Co.*, 189 F. 95 (103((C.C.S.D.N.Y. 1911) (L. Hand, J.), *aff'd in part and rev'd in part*, 196 F. 496 (2d Cir. 1912) (holding that the purified form of adrenalin—a compound existing in the human body—was patentable because the purification process transformed it into drug and therefore into “a new thing commercially and therapeutically”); *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991) (holding that naturally occurring DNA sequences constitute patentable subject matter when “purified and isolated” as compared to their natural form); *but see Association for Molecular Pathology, et al. v. United States Patent and Trademark Office, et al.*, 702 F.Supp.2d 181 (S.D.N.Y. 2010).

¹¹⁴ See Gitter, *supra* note 2, at 610 (reviewing the types of patents available to developers of biological products).

formulations containing the compounds,¹¹⁵ and (4) methods of using the biological compound in the treatment of illnesses.¹¹⁶ Since the natural course of development of most biologics first involves the identification, making and isolation of a biologic having therapeutic properties (not necessarily in that order), the first patent applications commonly seek to claim the biological API, closely related compounds and methods of making them and are filed very early in the development process,¹¹⁷ typically between the time immediately pursuant to the identification of the biological API and right before the beginning of clinical trials in human subjects.¹¹⁸ In other words, if the beginning of the R&D efforts is marked as the “0” time-point and clinical trials normally begin after 4-5 years of preclinical studies, then the filing of the first patent application pertaining to the biological product would normally occur between “development years” 1 and 4-

¹¹⁵ See Gitter *id.* Formulations are the compositions of the final product, namely the active pharmaceutical ingredient (“API”) and different pharmaceutically inactive ingredients (also known as “excipients”) having certain functions in the composition, e.g., stabilization, dissolution, adjustment of pH, filling, etc.

¹¹⁶ See Gitter *id.*

¹¹⁷ Cf. *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, 598 F.3d 1336 (Fed. Cir. 2010) (essentially abolishing method claims directed to mechanisms of action *per se*, namely as standalone claims independent from sufficient disclosure of compounds that are used to achieve the desired action as part of the 35 U.S.C. § 112 ¶ 1 written description requirement).

¹¹⁸ See *In Re Brana*, 51 F.3d 1560, 1567-1568 (Fed. Cir. 1995) (holding that an antitumor compound does not necessarily have to be tested *in-vivo* to fulfill the utility requirement under 35 U.S.C. § 101 and that *in-vitro* tests using cell-line models may be sufficient; stating that “[t]he stage at which an invention in [the field of biologics] becomes useful is well before it is ready to be administered to humans”); *In re '318 Patent Infringement Litigation*, 583 F.3d 1317, 1389 (Fed. Cir. 2009) (“results from animal tests or in vitro experiments may be sufficient to satisfy the utility requirement”). Notably, this estimated timeframe is confirmed by my findings that the average time period between the filing of the first patent applications pertaining to biological products and their approval by the FDA is about 3728 days, or 10.2 years. See *supra* note 106. Deducting the estimated 6-9 years of clinical trials and 1-1.33 years of processing of BLAs it appears that the timeframe of filing of the first patent applications covering biological products is about 0-3 years prior to the beginning of clinical trials.

A possible explanation to this patent filing strategy is that once a compound enters the stage of human trials it is exceedingly difficult to keep it as a trade secret and the early filing is meant to preserve the developer’s prospects of monopoly in any product that may result from its R&D efforts. Another explanation is that early filing of patent applications mitigates pressure from in-house scientists to be allowed to publish their scientifically significant findings in scientific literature.

5 (depending on the length of the preclinical trials stage).¹¹⁹ Patents generally expire 20 years from the filing date of the original application.¹²⁰ Thus, as a general proposition, the primary patents¹²¹ pertaining to biological products would be set to expire between “development years” 21-25,¹²² whereas the market exclusivity period pertaining to the products covered by these patents would expire around “development years” 23-28.

However, when comparing the term of statutory exclusivities to the term of primary patents, it is necessary to take into account patent term extensions that *one primary patent per FDA-approved product* may receive under 35 U.S.C. § 156.¹²³ If we make the most patent-term-favorable assumptions that virtually all first primary patents (i.e. the first primary patent to issue

¹¹⁹ Notably, the first patent application is not necessarily the first submission to the USPTO, which is frequently of a provisional application containing little more than preliminary data and a rudimentary concept of the invention and whose purpose is merely to “buy” the inventors another year for further development of their invention. *See* 35 U.S.C. §§ 111(b), 119(e). For further discussion of provisional applications *see* USPTO, Provisional Application for Patent, <http://www.uspto.gov/patents/resources/types/provapp.jsp>.

¹²⁰ *See* 35 U.S.C § 154. This expiration date may be adjusted to compensate for delays in the processing of the application by the USPTO, a filing of a terminal disclaimer with respect to the issued patent and time lost during the examination and approval of the BLA by the FDA. *See infra* Part IV.B.

¹²¹ For purposes of the discussion herein, a “primary patent” is defined as a patent issued from one of the first patent applications to be filed early in the R&D of the biological product and covering, typically, the biological API itself, its manufacturing and/or the first known methods of using it.

¹²² This calculation is based on adding the estimated 1-4 years from the onset of development—which is the period during which one could assume most early patents pertaining to a biological product would be filed—to the 20 year patent term.

¹²³ Under 35 U.S.C. §§ 156(a)(4), 156(c), 156(f)(2)(A), 156(g)(1), 156(g)(6), 21 U.S.C. § 355(i) and 42 U.S.C. § 262(j), the term of patents pertinent to biological products “shall be extended by the time equal to the regulatory review period for the approved product” *up to a total period of 14 years from the date of approval of the biological product but not exceeding 5 years*, whereas the “regulatory review period” is calculated as half the time in which the product was in clinical trials, plus the period it took the FDA to review and approve the BLA. *See id.*; *see also* Mossinghoff, *supra* note 26, at 190 (reciting and explaining the abovementioned patent term extension provisions and stating that “[t]he patent term restoration part . . . in title 35 of the United States Code . . . [consists of] very long, very complicated provisions . . . The length of the exclusivity periods are strictly arbitrary legislative numbers pulled out of the air.”).

for any given biological product) would merit an extension of 4-5 years,¹²⁴ then it is possible to argue that for any biological product there would be one patent whose term would be extended 1.5-2 years beyond the expiration of the 12-12.5-year market exclusivity period.¹²⁵ Thus, while generally the first patents covering biological products would expire within 21-25 years from the onset of development, under the above patent-term-favorable assumptions, one of the primary patents would expire within about 25-30 years from that date.¹²⁶ However, in reality not all primary patents are entitled to a patent term extension, as in some instances the term of primary patents already extends beyond 14 years from the date of FDA-approval. Thus, as I will argue in the next section, even with patent term extension, primary patents are expected to expire, on average, around 5-11 months subsequent to the expiration of the 12-12.5-year market exclusivity period under BPCIA.¹²⁷

¹²⁴ Given the length of clinical trials of biologics and the average 12-16 months needed for FDA review of BLAs, it is prudent to assume that the majority of biological products would merit the maximum patent term extension of half the clinical trials' period plus the time needed for FDA review of the application up to a maximum of 5 years. Basing the calculation on the estimated times brought herein, the term extension could be roughly estimated as equal to ½ of 6-9 years plus 1-1.33 years, namely 4-5.83 years. Given the upper limit of 5 years, a typical patent term extension period would be 4-5 years.

¹²⁵ Since under 35 U.S.C. § 156 patent term extension cannot extend the patent term beyond 14 years from the date of FDA approval of the product and the statutory market exclusivity under BPCIA extends for 12-12.5 years from that date, then, arguably, no patent term could be extended more than 2 years beyond the expiration of a twelve-year market exclusivity or 1.5 years beyond the expiration of a 12.5-year market exclusivity.

¹²⁶ This calculation is based on adding the estimated 4-5 years of patent term extension to the 21-25 years patent term from the inception of development. The calculation would be slightly different if we were to add 2 or 1.5 years to the statutory exclusivity period of 23 to 28 years, resulting in a similar patent term extending 25-29.5 years from the beginning of development.

¹²⁷ See *infra* Part IV.B.

B. Patent term vs. Market Exclusivity for Biologics—A Case Study

In order to test the validity of the above timeframe estimates and compare the term of patents pertaining to biological products with the term of market exclusivity that such products would receive under BPCIA, I calculated (1) the term of the first-to-issue primary patents¹²⁸ pertaining to seventy-nine already-approved biological products listed in Table 1¹²⁹ and (2) the hypothetical dates in which the market exclusivity in these products would have expired had these products been subject to BPCIA.¹³⁰ Based on these dates, for each of the first-to-issue primary patents identified I calculated the time from expiration of the patent to the end of the twelve-year market exclusivity in the product and then, based on the results received, the average time for the seventy-nine products between the end of the twelve-year market exclusivity and the expiration of the primary patent.¹³¹ According to these calculations, the average time difference between the end of the twelve-year market exclusivity in a biological product and the expiration

¹²⁸ See Table 1 included as Appendix A, note 248 and accompanying text. The patent term calculation was based on the various sections of patent law and includes any patent term extensions awarded to patents under the Hatch-Waxman Act as listed in the USPTO Listing of Patent Term Extensions under 35 U.S.C. 156, <http://www.uspto.gov/patents/resources/terms/156.jsp> and any patent term adjustments as reflected on the face of the patents and in the patent information available through the USPTO Patent Application Information Retrieval System (PAIR), <http://portal.uspto.gov/external/portal/pair>.

¹²⁹ The list consists of seventy-nine biological products for which primary patents could be identified, including sixteen out of the twenty-four best selling biological products in 2008 and excluding insulin and human growth hormone (hGH) products, for which generic (or “follow-on”) versions have already been approved by the FDA. See LaMerie Business Intelligence, *Top 20 Biologics 2008*, R&D Pipeline News—Special Edition 1/2009, Mar. 9, 2009 at 3-6 (including Enbrel, Remicade, Epogen, Rituxan, Avastin, Herceptin, Aranesp, Neulasta, Lantus, Avonex, Lucentis, Erbitux, Betaseron, Neupogen, Cerezyme, Synagis). Notably, the above selection criteria for the analyzed sample of seventy-nine biological products might, admittedly, reflect selection biases. At the same time, it is difficult to determine what would be considered a “representative sample” of biological products for the purpose of calculating the average length of primary patent life covering such products.

¹³⁰ See Appendix A, note 249 and accompanying text.

¹³¹ See Appendix A, note 251 and accompanying text. Notably, for purposes of the calculations herein, I refrained from making any assumptions regarding the potential addition of ½ year of market exclusivity for experimentation in pediatric populations. See *supra* note 86 and accompanying text.

of the first-issued primary patent is about 327 days.¹³² In other words, the average term of the first identified primary patents pertaining to the seventy-nine biological products listed in Table 1 extends about 11 months beyond the end of the twelve-year market exclusivity period in these products. Furthermore, if we add the extension of 6 months to the market exclusivity period (making it 12.5 years) for having a product tested and approved for pediatric use,¹³³ the average term of the first identified primary patents pertaining to the seventy-nine biological products listed in Table 1 would extend about five months beyond the end of the market exclusivity period in these products.

In conclusion, patents in the family of the original application¹³⁴ could be expected to expire roughly within 21-25 years from the onset of the development of the biological product¹³⁵ with one more patent expected to expire, on average, around 5-11 months after the period of market exclusivity under BPCIA. Thus, arguably, based on the above calculations, *the market exclusivity period under BPCIA would keep competition out of biologic markets, on average, for 5-11 months less than the average monopoly period afforded by primary patents on inventions*

¹³² The calculation of the average number of days between FDA approval and the expiration of the first-to-issue primary patent listed for each of the seventy-nine products is done as explained in note 251, adding the number of days for all seventy-nine products and then dividing by seventy-nine.

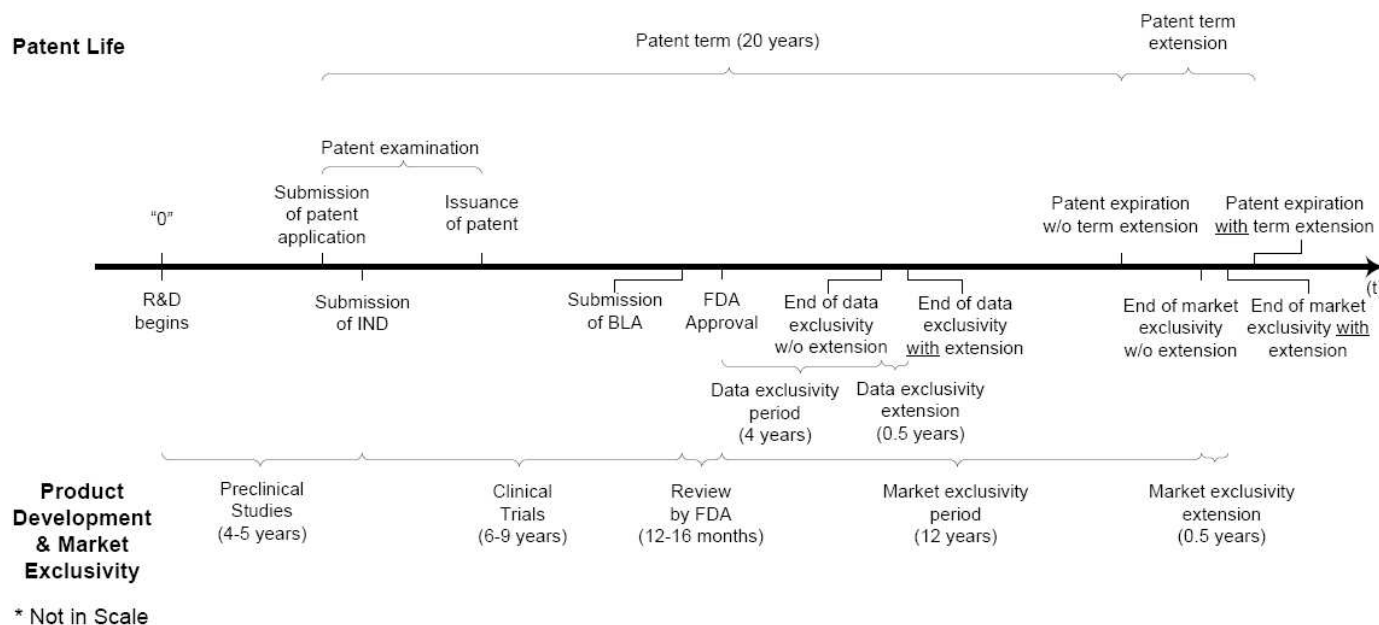
¹³³ See *supra* notes 86-87 and accompanying text.

¹³⁴ A “patent family” includes all divisional, continuation and continuation-in-part applications (and issued patents thereof) stemming from a certain earlier parent application. See USPTO, Manual of Patent Examination and Procedure §§ 201.04-201.08.

¹³⁵ See *supra* note 122 and accompanying text.

pertaining to the biological product.¹³⁶ These conclusions may be illustrated graphically as follows:

Figure 1:* Patent Term vs. Statutory Exclusivities in Biologics



These conclusions invite the question: what is the justification (if any) for this mostly overlapping protection of biological products under both BPCIA and patent law¹³⁷ and what implications might there be to this “double-tiered” protection?

¹³⁶ These conclusions are in accord with the rationale behind the twelve-year market exclusivity period for new biological products under BPCIA, namely, ensuring that original product developers would be able to monopolize their products for a period at least as long as that which their patents would have afforded them. *See supra* notes 72-74 and accompanying text. Importantly, these conclusions are only valid with respect to primary patents covering the “first wave of inventions” rather than to patents covering inventions resulting from continuing research.

¹³⁷ Disagreements regarding the length of patent protection are not uncommon, given the complexity of patent law and the dependence of such calculation on numerous factors (e.g., timing of filing of patent applications, the ramifications of various different types of extensions, the prosecution of the patents, etc.) However, even slight changes in the term of this patent or another do not change the fact that the effective result of BPCIA is the institution of “double monopoly protection” for biologics.

C. Patents vs. Statutory Exclusivities for Biological Products: A Public Policy Perspective

Comparing the rationales for granting statutory exclusivities with the patent theories discussed earlier, it appears that the reasoning behind both types of monopoly is quite similar if not identical, especially in the context of biologics. In a nutshell, the incentive-to-disclose and incentive-to-invent/invest patent theories emphasize patents' functional role of incentivizing the disclosure of existing inventions and the pursuit of further R&D activities leading to more inventions.¹³⁸ Taking a closer look at the rationales for granting statutory exclusivities reveals a highly similar picture. The purpose of statutory exclusivities in the context of pharmaceuticals is to provide assurance that developers of original biologics are able to reap the fruits of their investment, thereby ensuring the existence of sufficient incentive-to-invent/invest.¹³⁹ Thus, arguably, both patent and statutory exclusivities regimes (1) recognize developers' right to benefit from the fruit of their labor by creating means to exclude others from using the biologics they developed;¹⁴⁰ (2) enable only the developers to reap profits from the biological products for a certain period of time; and (3) encourage and require developers of biologics to disclose to the public the products they develop and their uses as a pre-requisite to the developers' ability to

¹³⁸ See *supra* Part II.A.

¹³⁹ See Kelleher, *supra* note 57, at 255 (“[the New Chemical Entity five year market exclusivity provision of the Hatch-Waxman Act] was meant to alleviate concerns that a generic pathway would prohibit innovators from realizing the benefits of their investments”); Wing Yan Tam, *supra* note 46, at 553 (“[t]he policy behind marketing exclusivities is to incentivize pharmaceutical research entities to engage in ambitious, cutting-edge research for the development of new drugs and to develop greater understanding about existing drugs.”); see also Grabowski 2009, *supra* note 5, at 2 (recognizing that both patents and statutory exclusivities “address the need for innovators to have some period of returns before imitators can enter the market with an abbreviated filing”).

¹⁴⁰ In the case of patents, these means to exclude take the form of letters of patent enforceable by courts while in the case of statutory exclusivities they entail direct exclusion of potential competitors from the market for the particular biological product.

receive exclusivity in their products.¹⁴¹ Accordingly, at least from a functional perspective, in the context of biologics, both patents and statutory exclusivities seek to achieve the same purpose and incentivize essentially the same behavior by inventors, investors and developers.

Accordingly, the goal of technological advancement in the area of biological products could be served by affording any kind of effective exclusivity guaranteeing sufficient profits to investors in R&D regardless of whether the product of such R&D would eventually fit in the strict mold of a “patentable invention” under patent law.¹⁴²

1. Why Patents May Not Provide Sufficient Protection to the Interests of Developers of Biological Products (and Therefore Would Fall Short as Means of Incentivizing the Developments of Biological Products)

The similarity of purpose and effect of statutory exclusivities and patent protection begs the question: why, if at all, is there a need for statutory exclusivities in addition to patents? The justification that is most frequently offered for making statutory exclusivities in biological products available in addition to patents is the insufficiency of patents alone for protecting

¹⁴¹ In the context of patents, disclosure takes place as part of patents’ specifications. In the context of statutory exclusivities, disclosure occurs in the submission of some publicly available information as part of the BLA. Thus, the incentive-to-disclose rationale is *inherent to the context of biologics* for the reason that it is impossible to commercialize a biologic without prior approval by the FDA, which can only be granted subsequent to the submission of information regarding the product, including such publicly available information about the nature of the product and its intended medical uses. In other words, the incentive to disclose information to the public about biologics exists regardless of any additional exclusivity that may or may not be granted to the products’ developers under patent law. Interesting questions remain, however, as to the extent of disclosure incentivized by patent and statutory exclusivities regimes with respect to manufacturing “know-how” and actual clinical data. For further discussion of these issues *see infra* Part IV.C.2(b) and note 160 ¶2 and accompanying text.

¹⁴² As early as the 1950s, Machlup already recognized that it is “monopoly grant” in general, rather than patent monopoly in particular, that is necessary to incentivize the risks taken by financiers of industrial application of certain technology. *See* Machlup, *supra* note 11, at 36-37 (“[t]he risks involved [in investment in technological R&D] may be too great to be undertaken except under the shelter of a monopoly grant”). According to this logic, statutory exclusivities would be no different than patents from the incentive-to-invest point of view.

proprietary interests in biological products.¹⁴³ Viewed in this light, in the context of biologics statutory exclusivities are sometimes referred to as “insurance policies” meant to protect the interests of developers of biological products where patents might fail in doing so.¹⁴⁴ There are several reasons for the insufficiency of patents as means of protecting the interests of developers of biological products and for why they would prefer a statutory exclusivities’ regime such as that which has been established by BPCIA.

(a) Acquiring Patents and Enforcing them Cost a Lot, Yet Patents Provide a Limited Degree of Legal Protection to Biologics

The patent system suffers from inherent shortcomings that make the investment in obtaining and enforcing patents a risky and highly uncertain prospect. The securing and enforcement of patent rights involve a long and tedious *via dolorosa* of intricate (and expensive) proceedings. They require compliance with complicated legal criteria such as “novelty,” “usefulness” and “non-obviousness” as well as a plethora of procedural and technical requirements stemming from centuries of litigation and patent prosecution.¹⁴⁵ This complexity,

¹⁴³ See *infra* Parts IV.C.1(a)-IV.C.1(d). Representatives of original biologics developers have made forceful assertions regarding the need for both statutory exclusivities and patent protection in biological products. See e.g. BIO White Paper, *supra* note 2, at 22 and 37 (arguing that “[a]s was the case in the Hatch-Waxman Act, it will be important to consider patent exclusivity, along with market exclusivity provided through the regulatory approval mechanism, as an integral part of the follow-on biologic approval framework” and that “any statutory pathway for the approval of follow-on biologics must contain an appropriate mix of patent-based and market/data-based exclusivity to ensure effective market protection to incentivize investment and innovation”).

¹⁴⁴ According to Grabowski and DiMasi, the purpose of statutory exclusivities is to provide investors “with an ‘insurance policy’ against the potential failings of patent protection for biologics.” See Grabowski et al., *supra* note 5, at 4; Grabowski & DiMasi 2009, *supra* note 5, at 8 (“[f]rom the standpoint of innovative firms, [statutory] exclusivity protection provides a back-up or insurance policy to the patent system”); BIO Data Exclusivity Position Paper, *supra* note 5, at 4 (“a 14-year period of data exclusivity serves essentially as an insurance policy that provides the innovator with some certainty of protection”).

¹⁴⁵ See Machlup, *supra* note 11, at 6 (“but just what an ‘invention’ is, and when it can be regarded as ‘novel’ and ‘useful,’ is not self evident. The questions of the ‘correct’ criteria of utility, novelty, and invention have been answered in many different ways, and the courts of several countries are constantly reconsidering earlier answers”). For a good exemplification of the intricacy of patent prosecution proceedings one need only consider the volume of

when combined with the high rate of patent invalidation in litigation,¹⁴⁶ creates uncertainty regarding the outcome of patent litigation and undermines the ability of developers and entrepreneurs to rely on patents as reliable means of securing their investment.¹⁴⁷ Machlup described the shortcomings of patents as follows:

The patent system lacks logic. It postulates something called ‘invention’ but in fact no satisfactory definition of “invention” has even appeared, and the courts, in their search for guiding rules, have produced an almost incredible tangle of conflicting doctrines. This confusion has led to extensive and costly litigation. Its critics have described the patent right as merely “something which has to be defended in the courts” and, because it may put the individual inventor at a disadvantage against the larger corporations, as “a lottery in which it is hardly worthwhile taking out a ticket.” The system, too, is wasteful. It gives protection for 16 years (or thereabouts) whilst in fact over nine-tenths of the patents do not remain active for the whole of this period . . . **It is almost impossible to conceive of any existing social institution so faulty in so many ways. It survives only because there seems to be nothing better.**¹⁴⁸

All of these shortcomings of the patent system appear to be further exacerbated in the context of pharmaceuticals in general and biologics in particular.¹⁴⁹ First, as I will later argue,

the USPTO’s Manual of Patent Examining Procedure (MPEP). See MPEP, 8th ed. (2001), available at <http://www.uspto.gov/web/offices/pac/mpep/mpep.htm>.

¹⁴⁶ See Michael Meehan, *Increasing Certainty and Harnessing Private Information in the U.S. Patent System: A Proposal for Reform*, 2010 Stan. Tech. L. Rev. 1, 1 (2010) (“[n]early half of litigated patents are invalidated”).

¹⁴⁷ See Grabowski 2008, *supra* note 5, at 482 (warning that “if the relatively few large success[ful biological products that make it through development and approval] experience increased uncertainty due to patent challenges and the potential for early entry of generic versions, higher risk-adjusted rates of return will be demanded by venture capital firms as well as in initial public offerings and secondary offerings in public markets, yielding fewer candidates that meet this standard.”); Grabowski & DiMasi 2009, *supra* note 5, at 9 (“[u]ncertainty about recoupment periods and the ability to earn a risk adjusted return on particular new product candidates will result in fewer of these candidates being taken forward into development.”).

¹⁴⁸ Machlup, *supra* note 11, at 44. Despite the fact that Machlup made these statements over 50 years ago – before the patent term was adjusted to 20 years from the date of filing and prior to the creation of the Federal Circuit – it appears that much of what Machlup described in 1958 remains true today in the context of biologics.

¹⁴⁹ See Grabowski 2009, *supra* note 5, at 2 (“[p]atents may provide less clear and less predictable intellectual property protection for biologics than for small molecule drugs”) and 4 (“there is a much higher probability now

due to some particular characteristics, biologics are subject to especially high barriers to patentability not existing in other areas of technology.¹⁵⁰

Second, the patent dispute resolution framework established by BPCIA would necessitate an even higher investment of resources by all of the parties involved.¹⁵¹ As discussed earlier, BPCIA sets up a highly complicated and elaborate framework for the resolution of patent disputes arising out of the filing of an application for biosimilar products.¹⁵² This framework would require potential adversaries to obtain extensive legal counseling¹⁵³ and, possibly, litigate numerous patent disputes in several different legal proceedings over a prolonged period of time.¹⁵⁴ Furthermore, protecting a single biological product normally involves more than one patent so it is prudent to assume that patent disputes arising in the context of biologics would not

than there was a decade ago that drugs will experience patent challenges and that they will occur much sooner after brand launch.”).

¹⁵⁰ See *infra* Part IV.C.1(b); See also BIO Data Exclusivity Position Paper, *supra* note 5, at 2-3 (arguing that patent law yields increasingly narrow patent claims to biologics).

¹⁵¹ See Laura A. Coruzzi, Jonathan A. Muenkel & Lynda Q. Nguyen, *The Crusade for Follow-On Biologics: The Next Wave of Pharmaceutical Patent Litigation?*, 2 No. 1 LANDSL 30, 31 (2009) (predicting that the passage of a framework for the approval of generic versions for biological products may “result in an influx of patent litigation in the field of biology”).

¹⁵² See *supra* notes 93-104 and accompanying text.

¹⁵³ BPCIA dictates that the parties involved in the patent dispute partake in an exchange of patent lists and statements of their respective legal positions, to be followed by negotiations aimed at the resolution of possible patent disputes prior to and in lieu of resorting to any legal action in court. See BPCIA § 7002(a) (codified as 42 U.S.C. §§ 262(l)(2)-262(l)(4)). Given these proceedings’ robustness, the necessary involvement of attorneys in these proceedings is unlikely to come at an insubstantial cost.

¹⁵⁴ The framework set up in BPCIA accounts for the possibility that patent disputes under BPCIA may involve several different legal proceedings spanning over the course of 8 years or more, beginning with the expiration of the data exclusivity period—four years after the approval of the original product—and ending with the conclusion of actions for declaratory judgment and/or injunction prompted by an advance notice of intent to market a biosimilar product given 180 days prior to the onset of marketing. See BPCIA § 7002(a) (codified as 42 U.S.C. §§ 262(k)(7)(B), 262(l)(6), 262(l)(8) and 262(l)(9)). Notably, the existence of patents covering the biological product would automatically trigger the BPCIA patent dispute resolution proceedings even if the patents are set to expire prior to the end of the market exclusivity period.

only entail several legal proceedings over a prolonged period of time, but would also involve several patents directed at different types of inventions.¹⁵⁵

Finally, the scope afforded to patents pertaining to biologics by courts is even more unpredictable than that of patents in general due to the uncertainty surrounding the application of the doctrine of equivalents to this relatively new area of technology.¹⁵⁶ Combining all of the above with the already increased likelihood of patent challenges characterizing the area of pharmaceuticals in recent years,¹⁵⁷ the prospect of utilizing patents to protect proprietary

¹⁵⁵ See Grabowski 2009, *supra* note 5, at 2-3 (“[b]iologics rely on multiple patents, including narrower product patents and process patents”); *supra* notes 113-116 and accompanying text. More patents represents a larger investment in prosecution and enforcement as well as increased uncertainty regarding the scope of the protected rights and the degree and extent of their enforceability.

¹⁵⁶ The doctrine of equivalents is a patent law construct meant to encompass within the scope of patent claims subject matter which does not squarely fall under the literal meaning of the claim but is nonetheless equivalent to the patented invention. The most common legal standard for equivalence is the “function-way-result” test according to which a product or process is deemed an equivalent where “the accused product or process performs substantially the same function, in substantially the same way, to achieve substantially the same result, as disclosed in the claim.” See *Abbott Laboratories & Astellas Pharma, Inc. v. Sandoz, Inc. et al.*, 566 F.3d 1282, 1296-1297 (Fed. Cir. 2009) (“[e]quivalency may also be proven where the differences between the invention as claimed and the accused product or process are insubstantial.”). Thus, for example, even if a generic biological API would not literally infringe the relevant compound claim, it could trigger an issue of equivalents if the two compounds would have substantially the same structure enabling them to achieve substantially the same result in substantially the same way or are otherwise only different in an insubstantial way. According to the Biotechnology Industry Organization (BIO), “[b]iotechnology is considered an unpredictable field because it is often not known how even a minor change may affect the structure, behavior and biological activity of a protein.” See BIO White Paper, *supra* note 2, at 28. Thus, if even a seemingly minor change to a biological compound may drastically affect its structure, the way it functions and/or its biological result, then it is possible to say that such minor changes in a biological compound would affect the “function-way-result” aspects of such compound in a “not insubstantial way,” which, in turn, would render the scope of equivalents in such a compound highly unpredictable. Accordingly, as recognized in the BIO White Paper, “there is no certainty that an innovator can obtain adequate patent protection covering variant proteins.” See BIO White Paper, *supra* note 2, at 28. See also Aljalian, *supra* note 168 at 55-57 and 66-72 (arguing that “[t]he application of the doctrine of equivalents in the realm of gene and protein patents, which appear to be the foundation of new medical breakthroughs, is highly significant . . . Thus there is debate over its applicability” and calling for limiting the applicability of the doctrine of equivalents in such patents).

¹⁵⁷ See Grabowski & DiMasi 2009, *supra* note 5, at 19 (“the trend in recent years has been for patent challenges to become much more frequent”).

interests of developers of biological products appears to be far from attractive, which may, in turn, result in a curbing of R&D.¹⁵⁸

Interestingly, these shortcomings of the patent system are “complemented” with claims that, at least in the context of biologics, patents do not serve their role as facilitators of disclosure of valuable information to the public.¹⁵⁹ Biotechnology patents have been accused of not providing sufficient disclosure to benefit the public and of revealing only piecemeal portions of certain technologies, which are useless in and of themselves and which could only serve as part of larger mechanisms to which the public is not made privy.¹⁶⁰

¹⁵⁸ See 2008 CRS Report, *supra* note 1, at 24 (“several experts maintain that defending patents may divert support from on-going innovation, especially in small companies that make up a significant portion of the biotechnology sector”).

¹⁵⁹ See *supra* Part II.A.1.

¹⁶⁰ See e.g. Sorscher, *supra* note 58, at 305 (“the patent for [biologics] may only cover early versions of the product produced in the laboratory setting, not the master cell lines and scaled-up industrial process used to produce the product eventually tested on patients and approved by the FDA. Firms can and do seek trade secret protection on these cell lines and processes, forcing follow-on manufacturers to start over after a long an expensive design process.”).

Arguably, the statutory exclusivities established under BPCIA would not do a better job at facilitating disclosure of meaningful/practical information to the public since the actual clinical data and manufacturing know-how submitted as part of the original BLA is considered proprietary and therefore not accessible to the public. See generally Letter from Prof. John C. Yoo to the Food and Drug Administration, Division of Dockets Management (Oct. 21, 2004), available at <http://www.gphaonline.com/sites/default/files/UC-Berkeley%20Professor%20Yoo's%20Analysis%20of%20the%20Takings%20Clause.pdf> (addressing the constitutionality of the FDA’s reliance on safety and efficacy conclusions reached in approval proceedings of original biological products for the approval of generic versions of such products and determining that it is not a taking of such (admittedly) proprietary information under the Fifth Amendment). Cf. generally Dinh, *supra* note 3, at 102-103 (arguing that drug developers have no property interest in the public fact that a certain drug was found to be safe and efficacious enough to be approved for marketing and because such reliance does not involve an actual disclosure of clinical data submitted by drug developers); Andrew Wasson, *Taking Biologics for Granted? Takings, Trade Secrets, and Off-Patent Biological Products*, 2005 Duke L. & Tech. Rev. 4, 30 (2005) (arguing that “it is unlikely that the approval of off-patent biologics originally approved under the [F]DCA would be a taking”); John C. Yoo, *Takings Issues in the Approval of Generic Biologics*, 60 Food & Drug L.J. 33, 43 (2005) (“[i]f FDA decided to use the knowledge acquired by a pioneer company in furtherance of a subsequent approval of a generic biologic drug, the agency likely would encounter no significant taking issue.”). Some commentators have argued that the FDA should make *full disclosure* to the public of safety and efficacy data relied on as part of approval proceedings of new pharmaceuticals. See e.g. Galbraith, *supra* note 205, at 712, 752-54, 762-767 (2009) (making a compelling argument in favor of “comprehensive disclosure of meaningful clinical trial data from all studies, regardless of

FDA-granted statutory exclusivities, on the other hand, are obtained and enforced automatically, as a by-product of the FDA approval proceedings,¹⁶¹ and their practice does not require their beneficiary to take any specific action.¹⁶² They also do not lend themselves to the skirmishes that characterize patent infringement disputes.¹⁶³ Thus, statutory exclusivities negate the need for long, cumbersome, expensive and uncertain proceedings such as those characterizing patent prosecution and enforcement, which makes statutory exclusivities highly appealing as means of protecting one's investment in technology.¹⁶⁴ Rather, statutory exclusivities provide a relatively predictable outcome in case of potential disputes, which, in

whether FDA approval is obtained or even sought"); *see also* *See Ruckelshaus v. Monsanto Co.*, 467 U.S. 986, 1005-1009 (1984) ("the Trade Secrets Act cannot be construed as any sort of assurance against internal agency use of submitted data during consideration of the application of a subsequent applicant for registration.").

¹⁶¹ As discussed earlier, statutory exclusivities are conferred "automatically" on recipients of FDA marketing approvals and thus, securing them requires *no direct additional investment* on the part of developers of biologics. Putting a biologic through all the tests and clinical trials necessary for approval by the FDA is an essential and unavoidable part of its approval for marketing. Therefore, the investment involved in obtaining FDA approval for biological products should be viewed as sunk costs, i.e. as a necessary expenditure that has to be invested regardless of the legal protection sought for the investment. Hence, the direct investment in obtaining a statutory exclusivity could be viewed as \$0 while obtaining and securing patents in related inventions would presumably involve additional costs. Similarly, the enforcement of patents would require the developers of original biologics to invest significant amounts in bringing lawsuits against infringers. As for statutory exclusivities, if anything, it would be the FDA that would bear the costs of litigating possible challenges of its decisions not to approve additional products for the treatment of a particular condition or having a certain chemical structure and not the developers of the original products.

¹⁶² Under BPCIA, potential competitors would be barred from even attempting to enter the market while the statutory exclusivities are in place because the FDA would be unable to accept for evaluation any application for a follow-on biological product prior to the expiration of the data exclusivity period or approve such applications prior to the expiration of the market exclusivity period. *See supra* notes 84-85 and accompanying text.

¹⁶³ As discussed earlier, statutory exclusivities are significantly less vulnerable to legal challenges than patents. *See supra* Part II.B. *See also* Brill, *supra* note 5, at 6 ("[p]atents can, and frequently are, subject to legal challenge and therefore contain some amount of uncertainty for the patent holder. Data exclusivity is not challengeable in court and therefore is not uncertain.").

¹⁶⁴ *See* Brill *id.* at 6. The application of statutory exclusivities would not be affected by the inherent uncertainty accompanying patent law, especially with regard to such matters as the application of the doctrine of equivalents, meeting of burdens of proof, "battles of experts," inequitable conduct and more.

turn, represents not only significant cost savings but also minimization of investors' risks, thereby creating a business environment favorable to investment in R&D.¹⁶⁵

(b) The 'Product of Nature' Doctrine and the Insufficiency of Patents as Means of Promoting Basic Research and Development in Biology and Biomedicine

There are various types of biologics for which patentability is limited and yet for which R&D is highly desirable from a public policy perspective.¹⁶⁶ In many of these instances, the impediment to patentability is the 'product of nature' doctrine according to which patents may only be granted for "nonnaturally occurring [articles of] manufacture or composition[s] of matter" that are "product[s] of human ingenuity."¹⁶⁷ In other cases, the obstacles may be the heightened standards of written description and enablement,¹⁶⁸ best mode¹⁶⁹ and utility¹⁷⁰ and

¹⁶⁵ In this respect, the legal certainty accompanying a regime of statutory exclusivities has a clear advantage over patents from an incentive-to-invent/invest public policy perspective.

¹⁶⁶ E.g. genes, naturally occurring nucleic acid sequences (DNA and RNA) which have not been fully sequenced, non-purified naturally occurring compositions containing antibodies, naturally occurring proteins and hormones and so forth. See Kelleher, *supra* note 57, at 256 ("the patentability of some biological materials is extremely narrow due to stringent specification and enablement requirements").

¹⁶⁷ See *Diamond v. Chakrabarty*, 447 U.S. 303, 309-310 (1980). According to the *Chakrabarty* Court

The laws of nature [and] physical phenomena . . . have been held not patentable. . . . Thus, a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. . . . Such discoveries are "manifestations of . . . nature, free to all men and reserved exclusively to none."

Id. at 309 [internal citations omitted]. The 'product of nature' doctrine bears particular relevance to the context of biologics because so many biological products are in fact naturally occurring molecules, e.g. human growth hormone, insulin, erythropoietin, etc. See 2008 CRS Report, *supra* note 1, at 3 n. 19, 13 (addressing the implications of the 'product of nature' doctrine on biologics).

¹⁶⁸ See e.g. *In re Argoudelis*, 434 F.2d 1390, 1392 (CCPA 1970) (requiring making a deposit of microorganisms to a publicly available depository as part of meeting the written description and enablement requirements under 35 U.S.C. § 112, first paragraph); *Fiers v. Revel*, 984 F.2d 1164, 1170 (Fed. Cir. 1993) ("[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself"); Natasha L. Aljalian, *The Role of Patent Scope in Biopharmaceutical Patents*, 11 B.U. J. Sci. & Tech. L. 1, 28-30 (2005) (arguing that "biotechnology has come to have greater written description and enablement requirements, and patents in this field have been required

other issues specific to the area of biotechnology.¹⁷¹ As a result, there is an ongoing concern that such impediments to patentability might hinder highly desirable R&D of some types of biologics by making them insufficiently attractive to potential investors.¹⁷²

Various solutions have been proposed over the years to ease this tension between the need to encourage “basic research” (i.e. research that is aimed at the discovery and understanding of natural phenomena) and patentability.¹⁷³ However, these solutions have usually been partial

to strictly comply with these requirements”); BIO White Paper, *supra* note 2, at 30-32 (arguing that biotechnology is subject to “strict written description and enablement” requirements); Wing Yan Tam, *supra* note 46, at 544-47 (reviewing issues pertaining to enablement of biological inventions and arguing that many patents pertaining to biologics may be invalid for lack of enablement). *See also generally* Karen G. Potter, *Getting Written Description Right in the Biotechnology Arts: A Realist Approach to Patent Scope*, 28 Biotechnology L. Rep. 1, 17 (2009) (describing the uncertainty surrounding the law of written description in biotechnological patents).

¹⁶⁹ *See e.g.* Gregory N. Mandel, *The Generic Biologics Debate: Industry’s Unintended Admission That Biotech Patents Fail Enablement*, 11 Va. J.L. & Tech 8, 66-77 (2006) (arguing that patents directed to biological products are generally not enabled as they do not provide sufficient detail to enable practicing the inventions in terms of manufacturing know-how).

¹⁷⁰ *See* John R. Thomas, CRS Report for Congress: An Examination of the Issues Surrounding Biotechnology Patenting and Its Effect Upon Entrepreneurial Companies, at 18-26 (2000) [hereinafter 2000 CRS Report] (addressing the application of the utility requirement under 35 U.S.C. § 101 to biotechnologies).

¹⁷¹ *See e.g. Amgen v. Chugai*, 927 F.2d at 1206 (“when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated.”). *See also* 2000 CRS Report, *supra* note 170 at 11-18 (addressing potential obstacles to patentability due to what the author describes as “ethical concerns”).

¹⁷² One such type of research involves the identification of particular genes and naturally occurring mutations in the human genome. Among the most prominent types of genetic diseases whose exact genetic background remains unknown at this time are: asthma, various types of cancer, epilepsy and many more. *See* National Heart Lung and Blood Institute, *What Causes Asthma?*, http://www.nhlbi.nih.gov/health/dci/Diseases/Asthma/Asthma_Causes.html (“[r]esearchers think a combination of factors (family genes and certain environmental exposures) interact to cause asthma to develop”); National Cancer Institute, *Cancer Genetics Overview PDQ—Introduction*, <http://www.cancer.gov/cancertopics/pdq/genetics/overview/HealthProfessional/page2> (“[the] expanding knowledge [of cancer genetics] has implications for all aspects of cancer management, including prevention, screening, and treatment”); National Institute of Neurological Disorders and Stroke, *NINDS Epilepsy Information Page*, <http://www.ninds.nih.gov/disorders/epilepsy/epilepsy.htm> (“[r]esearchers are working to identify genes that may influence epilepsy”).

¹⁷³ For example, courts have created an exception for naturally occurring compounds if such compounds are “purified and isolated.” *See supra* note 113.

at best and, thus far, have failed to bring a conclusion to the debate over the patentability of specific types of biologics.¹⁷⁴

Contrary to the seemingly arbitrary and stringent requirements for obtaining a patent in the context of biologics, the statutory exclusivities regime set up by BPCIA does not give rise to similar impediments. Rather, it facilitates granting statutory exclusivities independent of external criteria such as “patentability” and depends only on the FDA’s finding of biological products as sufficiently safe and effective.¹⁷⁵ Thus, the statutory exclusivities regime established by BPCIA would incentivize *any* kind of R&D project that may eventually lead to biological products regardless of its patentability, including research that may lead to the discovery of naturally occurring and/or non-isolated biological compounds.¹⁷⁶

¹⁷⁴ A recent example of an ongoing ambiguity of the patentability of biologics is the re-heated debate regarding the patentability of naturally occurring DNA sequences (e.g. genes) and obvious variations thereof (e.g. cDNA, diagnostic products thereof, etc.). See *Assoc. for Molecular Pathology, et al. v. United States Patent and Trademark Office, et al.*, --- F.Supp.2d ---, 2010 WL 1233416 (S.D.N.Y.), 94 U.S.P.Q.2d 1683 (holding that DNA sequences are unpatentable subject matter even in their purified form because they are not “markedly different” from native DNA and that methods of analyzing DNA strands for certain sequences not tied to a particular apparatus/machine are equally non-patentable subject matter).

¹⁷⁵ See discussion *infra* Part IV.C.1(a)0.

¹⁷⁶ A notable exception to the broad applicability of statutory exclusivities and their potential as means of incentivizing R&D in biomedical technology exists in relation to the development of means of diagnosing certain diseases, including by using identified DNA and RNA sequences. For the reasons mentioned above, newly identified genes and diagnostics thereof are currently held unpatentable. See *supra* note 174. However, they also seem to not fall under the definition of biologics under PHSA § 351(i) (*see supra* note 2). Nonetheless, genetic diagnostics have an important role in the prevention and treatment of certain diseases and genetic predispositions which could not have otherwise been detected. For example, the tests for the presence of mutations in the BRCA1 and BRCA2 genes associated with increased risk of developing breast and ovarian cancers, while not serving as means of preventing such cancers *per se*, assist in recognizing the need for medical surveillance and preventive treatment for individuals having these mutations. See National Cancer Institute, *Fact Sheet: BRCA1 and BRCA2: Cancer Risk and Genetic Testing*, <http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA>. Thus, it is desirable to grant some form of statutory exclusivities—even if shorter than those afforded by BPCIA—in genetic diagnostics so as to incentivize research leading to the development of such diagnostics.

(c) Patents Provide Insufficient Protection to Biological APIs and the Processes of Making Them

Patent compound claims¹⁷⁷ and claims directed to methods of making them might prove ineffective in protecting particular biological compounds.¹⁷⁸ As explained earlier, biological compounds are highly complex molecules and are often made of hundreds, sometimes thousands, of building blocks arranged in intricate three-dimensional structures.¹⁷⁹ Thus, biological compounds and the processes of making them normally lend themselves to an enormous number of potential variations, which could be used for “designing-around” patent claim limitations in order to yield highly similar compounds or highly similar processes of making them.¹⁸⁰

Moreover, for the reasons discussed, the doctrine of equivalents would probably not provide effective means for encompassing such “design-arounds” within the scope of the

¹⁷⁷ Compound claims are patent claims drafted specifically to cover a particular chemical or biological compound or a group of particular compounds defined by structure, function and/or characteristics (e.g. melting point, X-ray diffraction pattern, solubility, density, etc.).

¹⁷⁸ See Kelleher, *supra* note 57, at 256 (“[t]he complexity of most biologics may allow a biogeneric manufacturer to design around an innovator’s patents[sic], but still secure regulatory approval through its “biosimilarity” to the pioneer biologic”); Grabowski et al., *supra* note 5, at 4 (“[p]atent protection alone may be insufficient for biologics in the context of biosimilars”).

¹⁷⁹ See *supra* note 2.

¹⁸⁰ See Gitter, *supra* note 2, at 612 (explaining that generic versions of biologics “might be sufficiently similar to the innovator biologic to rely on the FDA’s findings of safety and effectiveness for the innovator product, but at the same time prove different enough from the innovator product to avoid a patent infringement claim”); Jim Hollingshead & Rob Jacoby, Avoiding No Man’s Land: Potential Unintended Consequences of Follow-On Biologics, at 16 (2009), available at [http://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/us_lshc_avoiding%20no%20man's%20land_FOB_033009\(1\).pdf](http://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/us_lshc_avoiding%20no%20man's%20land_FOB_033009(1).pdf) (“many industry participants are concerned that innovators’ patents will prove relatively easy to circumvent. The very size of these molecules opens the possibility that a very small change to the molecule that preserves the core design . . . could circumvent the IP of the innovator company without technically infringing on its patent. Similarly, it is theoretically possible that [a generic manufacturer] could create a nearly identical molecule through a different process, and again be deemed technically to not be in violation of patents.”); BIO Data Exclusivity Position Paper, *supra* note 5, at 1 (discussing why biologics are susceptible to “design-arounds” and negative consequences thereof).

relevant claims.¹⁸¹ Given the innumerable possibilities of “design-arounds” existing for many biological compounds and the general unpredictability of the results of even minor changes to biological compounds, the application of the doctrine of equivalents to biotechnological inventions might prove extremely difficult.¹⁸² Even if we assume that the changes to the biological compound do not substantially affect the way it achieves a “substantially same” result, there would still remain the difficult question: what is “substantial structural similarity” in biologics for equivalence purposes? Apparently, the likelihood of establishing infringement of a biological compound claim under the doctrine of equivalents (at least at this point in time) is low at best, making it easier for generic manufacturers to enter the market before developers of original biologics had a chance to reap the profits that would make their efforts worthwhile.¹⁸³

¹⁸¹ See *supra* note 156. In view of the size of some proteins, it is quite possible that generic manufacturers could develop proteins that would be substantially structurally different from the original biological compound and yet have biological activity identical or highly similar to that of the original compound and therefore fall under the definition of “biosimilar” under BPCIA. See also Grabowski 2009, *supra* note 5, at 2-3 (“[b]iologics rely on multiple patents, including narrower product patents and process patents that may be more vulnerable to inventing around than small molecule product patents . . . it is possible that biosimilars may be different enough not to infringe on patents, but similar enough to qualify for an abbreviated approval pathway.”); Potter, *supra* note 168, at 14-15 (“[i]n practice, the Courts are reluctant to apply [the doctrine of equivalents] in biotechnology cases . . . It is far from certain how much variation in a protein a court would deem to be an “insubstantial” change. In sum, the [doctrine of equivalents] is so restrictive as to ‘eviscerate the applicability and potency of the [doctrine of equivalents] in almost all imaginable situations’”).

¹⁸² See Marr, *supra* note 57 (“[b]ecause biosimilars aren’t exactly duplicates of the original drugs, they don’t violate the original drug’s patent, enabling legal distribution before patent expiration.”); BIO White Paper, *supra* note 2, at 30 (explaining that two structurally different proteins could be biologically equivalent and still there would be no patent infringement); Vernon *et al.*, *supra* note 4, at 69 (arguing that it would be easy to “design around” biologics to avoid patent infringement violations while maintaining biosimilarity to an original biological product and that “[t]his artifact of intellectual property rights law places a greater emphasis on [statutory] exclusivity provisions for biologic products”). But see FTC Report, *supra* note 5, at vi (“there is no evidence that patents claiming a biologic drug product have been designed around more frequently than those claiming small-molecule products.”); Potter, *supra* note 168, at 1, 14-15 (describing a hypothetical case in which strict written description requirements make a patentee narrowly claim its invention thereby “inviting” imitations that do not fall within the scope of the invention as claimed).

¹⁸³ The author is not aware of any final court decision finding infringement of a biological compound claim under the doctrine of equivalents. Cf. *Amgen v. Hoechst*, 126 F.Supp.2d 69, 132-35 (D. Mass 2001) (finding that a patent claim for a 165 amino-acid erythropoietin was infringed under the doctrine of equivalents where the allegedly

The statutory exclusivities framework established under BPCIA would not give rise to such potential uncertainties and would eliminate the need to litigate altogether. The BPCIA statutory exclusivities' framework institutes a clear choice: if one wishes to rely on a previous FDA approval of a certain biological product without having to invest the vast amounts of money necessary in order to obtain approval of her own product, she would have to wait until the expiration of the relevant statutory exclusivity periods.¹⁸⁴ Under a statutory exclusivities regime, a generic manufacturer need only seek to obtain approval for its product to trigger the statutory exclusivity bar forbidding the FDA from approving its application regardless of whether or not the biological compounds are similar enough to be used interchangeably and what their degree of similarity is.

(d) Patents Provide Poor Protection to Biologics' Manufacturing Know-How

For many biologics, one of the most difficult and important aspects of bringing the product to the market is the development of manufacturing know-how.¹⁸⁵ However, for various reasons, know-how is especially difficult to protect under patent law. First, viewed through a

infringing molecule had only one more amino acid on the C terminus and achieved substantially the same clinical result in the same way and holding that there was no prosecution history estoppel) *rev'd* 457 F.3d 1293, 1308-12 (Fed. Cir. 2006).

¹⁸⁴ Notably, the possibility of approval of two parallel, potentially identical APIs for treatment of the same medical condition raises the separate issue of inefficiencies involved in parallel development of pharmaceutical products. A possible way of avoiding the waste of resources associated with such situations—at least those resulting from the respective developers' unawareness of the competing project—would be to have the FDA publish preliminary details regarding INDs it receives.

¹⁸⁵ See BIO White Paper, *supra* note 2, at 3 (explaining some of the difficulties involved in the manufacturing of biological compounds and their susceptibility to changes in manufacturing processes).

patent-law prism, the majority of manufacturing techniques are “well known in the art.”¹⁸⁶ Thus, the manufacturing recipes of most biological products could, arguably, be developed through ‘routine experimentation’ and would therefore be obvious under 35 U.S.C. § 103(a).¹⁸⁷ Second, as explained earlier, patent claims covering manufacturing processes could, and often are, “designed-around,” namely, evaded by making the same products in a different way, thereby rendering them irrelevant to protecting the substantial investment involved in the development of manufacturing know-how.¹⁸⁸

A grant of statutory exclusivities under BPCIA, on the other hand, would not require disclosure of manufacturing know-how to third parties (e.g. generic manufacturers).¹⁸⁹ Similarly, third parties would not be able to circumvent statutory exclusivities under BPCIA by “designing around” the protected products (at least not if the applicant wishes to rely on the original product for approval of its own generic version thereof).¹⁹⁰

¹⁸⁶ I.e. “well known” to persons of ordinary skill in the pertinent forms of art, such as molecular biology, biochemistry, etc.

¹⁸⁷ See *Ritchie v. Vast Resources*, 563 F.3d 1334, 1337 (Fed. Cir. 2009) (“[a]mong the inventions that the law deems obvious are those modest, routine, everyday, incremental improvements of an existing product or process that confer commercial value . . . but do not involve sufficient inventiveness to merit patent protection. This class of inventions is well illustrated by efforts at routine experimentation [where] method[s] of creation are well known, making successful results of the experimentation predictable.”).

¹⁸⁸ See Grabowski 2009, *supra* note 181 and accompanying text; see also BIO White Paper, *supra* note 2, at 32 (“[i]t is rare that a patented process of chemical synthesis will be able to block any and all means of producing the product”).

¹⁸⁹ See *infra* note 160 ¶2.

¹⁹⁰ See *supra* note 184 and accompanying text.

2. Why Concurrent Patent and Statutory Exclusivities Protection in Biological Products Might Have Undesirable Ramifications

In view of the above, it is not surprising that developers of biological products advocated vehemently in favor of long statutory exclusivity periods for original biological products.¹⁹¹ However, even though the literature is replete with arguments in favor of making statutory exclusivities available to biological product developers in addition to patents,¹⁹² the author is not aware of similar arguments having been made regarding a supposed need for patent protection *in addition to and concurrent with* the term of statutory exclusivities such as those provided under BPCIA; nor is the author aware of any justification for affording such protection.¹⁹³ In other words, no one seems to argue that statutory exclusivities, while they last, provide insufficient protection to the interests of developers of biological products such that they should be supplemented by patent protection. Rather, it appears that affording protection under both patent and statutory exclusivities regimes *while both of them are in effect* is likely to have undesirable ramifications.

¹⁹¹ See e.g. Grabowski 2009, *supra* note 5, at 3 (listing the advantages of statutory exclusivities and how they would remedy the shortcomings of patents in the context of biologics).

Arguably, the most straightforward way of addressing the inadequacy of the patent system for protecting biotechnological inventions would be to “fix” the patent system itself, namely by tailoring specific solutions that would encompass the type of product of biotechnological research and development activities that policy-makers seek to incentivize within the scope of what patent law would deem patentable subject matter. However, this route would not be preferable to statutory exclusivities because such highly specific biotechnology-oriented solutions might increase the transaction costs involved in obtaining and enforcing biotechnology patents, which, as explained above, is an already expensive and highly uncertain prospect.

¹⁹² See e.g. references cited *supra* note 5.

¹⁹³ As explained earlier, statutory exclusivities would negate the need for patent protection at least for the underlying biological compounds, the methods of making them and the initially approved methods of using them.

(a) Concurrent Protection by Both Patents and Statutory Exclusivities
Would Likely Lead to a Waste of Societal Resources

The enforcement of patents is an expensive prospect not only for the individual parties involved but also for society at large. Patent systems require substantial investment in education and training necessary to administer patent prosecution and litigation.¹⁹⁴ Moreover, maintaining a patent system with all its numerous elements, including a patent office, the various tribunals partaking in the administration and enforcement of patent laws¹⁹⁵ and highly trained personnel¹⁹⁶ requires a significant ongoing investment of societal resources.¹⁹⁷ Thus, the investment of resources in the enforcement of patent rights where statutory exclusivities already cover biological products would constitute a waste of the relative portion of societal resources (out of the entire societal investment in maintaining and administering a patent system) which is necessary to facilitate such enforcement.¹⁹⁸

¹⁹⁴ Hypothetically, had these resources not been invested in this manner they could have been invested in other, equally or possibly more socially beneficial avenues.

¹⁹⁵ E.g. the Board of Patent Interferences and Appeals and federal courts.

¹⁹⁶ E.g. judges, administrative judges, patent examiners and all their professional and administrative staff.

¹⁹⁷ Notably, the administration of the patent dispute resolution scheme established in BPCIA would require even further investment of societal resources such as those described herein. *See* further discussion of the BPCIA patent dispute resolution scheme *supra* Part IV.C.1(a).

¹⁹⁸ To clarify: the argument here is not that the entire societal investment of resources in the creation and maintenance of a patent system constitutes waste, but rather that the relative portion of such an investment which is necessary to support the handling of patent disputes as they pertain to biological products *which are being covered by statutory exclusivities under BPCIA* would be wasteful.

(b) Concurrent Protection by Both Patents and Statutory Exclusivities
Would Give Rise to Unnecessary and Avoidable Risks of Abuse

Monopoly—any monopoly—creates an inherent risk of abuse.¹⁹⁹ Thus, affording patent protection for biological products in parallel to FDA-instituted exclusivities would likely increase the risk of occurrence of abuse by developers of biological products in a variety of ways and disserve the public interest that both regimes were created to promote.²⁰⁰ Such abuse might result in an anti-competitive impact on incentives-to-invent/invest in biologics’ R&D, which would, almost inevitably, diminish public access to biological products.²⁰¹

BPCIA accounts for the risk of abuse of statutory exclusivities by specifically and explicitly disallowing grants of market and data exclusivities under certain circumstances. First,

¹⁹⁹ Machlup defines “abuse” as a situation where “the social objectives which [the monopoly] is supposed to serve are not promoted but rather jeopardized by the way it is used . . . when the temporal, functional, or material limits of the monopoly intended by the [monopoly] grant are overstepped and the actually achieved monopolistic control is extended in time, in scope or in strength.” See Machlup, *supra* note 11, at 10.

²⁰⁰ For example, numerous commentators have expressed concerns regarding patent abuse practices commonly referred to as “evergreening.” See e.g. Laurence J. Kotlikoff, *Clearing the Way to Low-Cost Biogenerics*, Boston Globe, Oct. 26, 2008, available at http://www.boston.com/bostonglobe/editorial_opinion/oped/articles/2008/10/26/clearing_the_way_for_low_cost_biogenerics/ (warning against granting developers of original biologics 12-14 years of statutory exclusivity alongside with patent protection and arguing that such protection would increase the risk that developers of original biologics would attempt to evergreen their biological products). According to Katlikoff, evergreening is “mak[ing] relatively minor changes to existing products in order to restart their monopoly protection clocks. These changes include changing the medication strength of pills . . . changing the form of medication (e.g., switching from pill to capsule), modifying the method of delivery (e.g., from injection to inhalation), expanding indications (applying the medicine to additional conditions), pegylation (which has the effect of reducing doses per time period via time-release mechanisms), and glycosolation[sic] (adding sugar molecules to the medication).” Katlikoff, *supra* note 5, at 9. See also Brill, *supra* note 5, at 7 (“[e]vergreening is a process whereby the holder of the patents for a biologic drug, using incremental changes to its original product, is able to shift the market to a newer product so as to limit a generic competitor’s market opportunity”).

²⁰¹ See Machlup, *supra* note 11, at 10-11 (“[p]atentees may succeed in extending the time period of control [e.g.]. . . through incomplete disclosure, making it impossible for those without special “know-how” to use the invention even after expiration of the patent; . . . through the successive patenting of strategic improvements of the invention which make the unimproved invention commercially unusable after expiration of the original patent . . . The patentee may succeed in extending the scope and strength of the monopoly beyond that intended by the law”), 28 (reviewing different arguments made by others that patents have been misused in various ways to inhibit fair and free competition regardless of efficiency) and 31 (quoting Edwards’s statement that “[there] are cases in which one enterprise has held control through patents [of an industry] for periods as long as half a century”).

BPCIA stipulates that applications for the approval of biologics that are “supplements” to an original BLA cannot re-trigger the market and data exclusivity provisions.²⁰² Second, BPCIA determines that applications filed by the same manufacturer or its “licensor, predecessor in interest, or other related entity” would not merit data or market exclusivity if the application is merely for a “modification to the structure of the biological product that does not result in a change in safety, purity, or potency.”²⁰³ Finally, under BPCIA, an application filed by the same manufacturer for a non-structural change of the biologic and “that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength” would, similarly, not award the manufacturer with an exclusivity period on top of that already awarded for the original biological product.²⁰⁴

²⁰² See BPCIA § 7002(a) (codified as 42 U.S.C. §§ 262(k)(7)(C)(i)).

²⁰³ See BPCIA § 7002(a) (codified as 42 U.S.C. §§ 262(k)(7)(C)(ii)(I)).

²⁰⁴ See BPCIA § 7002(a) (codified as 42 U.S.C. § 262(k)(7)(C)(ii)(II)). Notably, these provisions leave open the possibility of granting new data and/or market exclusivity terms for approval of applications for biological products submitted by the same manufacturer that entail a structural change to an original biological product and that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength. Yet, arguably, such re-triggering of the exclusivity period is justifiable since the manufacturer would have to put the biological product through what essentially would be a new approval process, including full blown clinical trials, and will therefore need to “re-invest” in R&D of what may well be viewed a new and different biological product. Notably, the BPCIA anti-evergreening provisions are in accord with Prof. Katlikoff’s recommendations for such measures. See *supra* 5 at 9 (proposing to award full monopoly protection only for the discovery and marketing of a new biologic).

By not affording additional statutory exclusivity for approval of additional indications of the same biological product, the statutory exclusivity scheme created by BPCIA differs from that of the Hatch-Waxman Act in that BPCIA does not incentivize additional clinical research leading to the approval of the same biologic for the treatment of additional medical conditions. See discussion of the Hatch-Waxman Act *supra* note 29 and accompanying text. In providing such exacting criteria for the grant of statutory exclusivities for already-approved drugs, BPCIA might actually curb much needed follow-up research of already-approved biological products, especially with relation to indications that require more complicated or elaborate R&D efforts which, as such, tend to be “pushed back” for later approval, once more easily provable medical benefits of the biological product have already landed it a “right of passage” into the market from the FDA.

Patents, on the other hand, do not seem to have the same kind of safeguards against abuse and remain relatively susceptible to evergreening.²⁰⁵ Furthermore, the elaborate patent dispute resolution scheme established in BPCIA might also, conceivably, give rise to different types of abuse similar to those that have been affected under the Hatch-Waxman Act.²⁰⁶ Thus, protecting biological products under patent law in addition to the statutory exclusivities framework available under BPCIA would create an opening for abuses of the patent system that would delay the entry of generic biologics into the market.

3. Biological Products Should Not Receive Concurrent Protection Under Both Patent Law and the Statutory Exclusivities Afforded under BPCIA

The conclusion from the discussion thus far is that concurrent protection of biologics under both patent and statutory exclusivities regimes is not only unnecessary but also undesirable. Rather, it would be preferable that any particular biological product be subject to protection under only *either* of these regimes, namely, BPCIA instituted statutory exclusivities *or* patents covering the underlying inventions pertaining to the biological product.

²⁰⁵ See Christine D. Galbraith, *Dying to Know: a Demand for Genuine Public Access to Clinical Trial Results Data*, 78 Miss. L.J. 705, 759 (2009) (“pharmaceutical companies have recently employed a wide variety of “evergreening” strategies to artificially extend the date a medication officially goes off patent”). A comprehensive review of the numerous possible “methods” of patent abuse and “evergreening techniques” in the context of biologics is beyond the scope of this article. Yet, for illustrative purposes it is worth mentioning a prominent example, namely when developers of original pharmaceutical products obtain patents on new methods of using an original biological product in combination with other pharmaceuticals, whereas the latter are enumerated in the patient prescribing information (PPI) for the original pharmaceutical products and then asserting inducement of infringement claims against generic manufacturers using the same PPIs (in accordance with FDA requirements) with their generic versions of such products.

²⁰⁶ See e.g. FTC, *Generic Drug Entry Prior to Patent Expiration: An FTC Study* (2002) (describing several types of patent abuse “techniques” used to keep generic competition off the market); see also FTC Report, *supra* note 5, at viii (“early start [of pre-approval litigation] does not guarantee early resolution . . . based on the experience under Hatch-Waxman, a pre-approval patent resolution process also is likely to lead to consumer harm . . . [by using] the pre-approval patent regulations to delay generic entry. In addition, generic and branded competitors have entered into “pay-for-delay” patent settlements that delay entry, not encourage it.”). Arguably, similar abuses could occur under the pretext of patent dispute resolution under BPCIA.

As explained earlier, statutory exclusivities have numerous advantages over patents.²⁰⁷ At least in the context of biologics, patents are a cumbersome, inefficient and often ineffective way of “promot[ing] the Progress of Science and useful Arts.”²⁰⁸ FDA granted statutory exclusivities, on the other hand, appear to be more comprehensive and easily enforceable, would significantly reduce costs involved in litigation, are less prone to abuse and would create legal certainty that is currently missing from the protection of technological innovation under patent law.

Furthermore, statutory exclusivities guarantee that only “worthy technologies” are granted monopolies. A constant concern in the context of technological advances is that monopoly grants may be squandered on “unworthy” technologies. For instance, it is not uncommon that inventions that lack any value to society are granted patents just because they happen to “satisfy” the requirements of patent law.²⁰⁹ As opposed to the patent examination process, which mostly utilizes standards not directly relevant to any particular technology, evaluation of new technologies by specialized agencies directly gauges the “social worth” of such technologies.

The FDA’s expertise and understanding in the area of biologics enables it to evaluate the potential medical benefits of biologics and weigh them against possible risks, thereby directly

²⁰⁷ See *infra* Part IV.C.1.

²⁰⁸ U.S. Const. Art. I § 8 Cl. 8.

²⁰⁹ Examples of what may be described as ridiculous patents covering socially worthless technologies are never in shortage. See e.g. <http://totallyabsurd.com/>.

determining the true societal value of specific biological products.²¹⁰ On the other hand, the patent system utilizes an array of “surrogate” or “proxy”—arguably irrelevant—standards to indirectly appraise the societal value of advancements, including biological products.²¹¹ Thus, at least in the context of biologics, a statutory exclusivities regime has an economic advantage over a patent regime as it is more likely to guarantee that monopolies are only awarded for “socially valuable” technologies.

4. A Proposed Amendment to Limit Patent Protection Where BPCIA Statutory Exclusivities are in Force

As discussed above, in the area of biologics, a statutory exclusivities regime is preferable to a patent regime. To avoid the negative ramifications of concurrent protection by both statutory exclusivities and patents, it is advisable that upon the onset of the statutory exclusivity period under BPCIA, developers of the approved products would no longer be able to enforce their patents as they pertain to the biological product *as approved* against generic manufacturers applying for the approval of generic versions of such products (“proposed amendment”).²¹²

²¹⁰ Direct examination by the FDA presumably guarantees that pharmaceuticals only receive monopoly via statutory exclusivities based on the criterion of whether they carry sufficient benefit to the public health *per se* rather than based on surrogate criteria for measuring their social worth, which may or may not guarantee that they actually convey any benefit to the public.

²¹¹ E.g. novelty, nonobviousness, written description, enablement, and more. *See* 35 U.S.C. §§ 101 *et seq.* The FDA evaluation is directed at the crux of the issue of benefit for the public, namely, whether the biological product is safe and efficacious enough to be approved as a medicine and therefore merits statutory exclusivity, regardless of whether or not a hypothetical person of ordinary skill in the art would have found it obvious or in compliance with other seemingly irrelevant criteria enumerated in patent law.

²¹² One way of achieving this result would be to amend Title 35 of the U.S. Code to limit section 271 so that it would create causes of action against generic applicants under BPCIA only if no statutory exclusivity under BPCIA is in effect with relation to the product covered by the patent whose enforcement is sought. A possible “softer” version of such a sweeping prohibition of enforcement of pertinent patents is to have developers of biological products elect *how* to protect their proprietary interests in their products, namely by choosing to benefit from the statutory exclusivities scheme afforded under BPCIA *or* having the ability to enforce their patents covering the underlying technologies in the approved biological product against generic applicants. To implement this “softer”

Importantly, this proposal would “strip” biological products of any additional period of protection under their primary patents subsequent to the expiration of the market exclusivity under BPCIA.²¹³ The potential loss²¹⁴ of this additional protection under patent law (flawed and partial as it may be²¹⁵) is justified because it reflects *payment for insurance embodied in the*

version of the proposed amendment, BPCIA could be amended to stipulate that the FDA would refrain from taking the actions related to the approval of generic versions of the biological products as prescribed under BPCIA § 7002(a) (codified at 42 U.S.C. § 262(k)(7)) only pursuant to a commitment by a BLA applicant to be estopped from enforcing its patents pertaining to the approved biological product against such generic applicants and/or *so long as* developers of biological products do not seek enforcement of their patents covering inventions pertaining to their biological products against parties seeking approval for generic versions of such product in accordance with BPCIA. See *supra* notes 84-85 and accompanying text. This “softer” version may circumvent possible challenges of the proposed amendment as an unconstitutional taking of one’s proprietary rights in its patents in violation of the Fifth Amendment of the Constitution. Importantly, this amendment is not meant to prevent developers of biological products from enforcing their patents against later applicants seeking approval *not* under BPCIA. Namely, under no circumstances would developers of biological products be unable to sue for infringement of their patents where a competitor might seek FDA approval of the same biological compound for the treatment of the same medical condition by conducting their own clinical trials, i.e. *without* relying on the approval of the original biological product under BPCIA.

A possible question is why leaving things the way they are, namely “for the market to take care of,” would not provide a sufficient and satisfying solution to the problems discussed above arising out of affording double protection to original biological products under both patent and statutory exclusivities regimes. Arguably, if patents are “so deficient” as a means of protecting one’s proprietary interests in biological products that alternative means – completely outside of patent law – are necessary to incentivize R&D of biologics, then developers of original biological products would be unlikely to seek or pursue enforcement of any patents covering their biological products and the whole issue of double protection would be moot. However, the need for the proposed measure limiting the protection afforded to original biological products is the risk of *abuse* of patent law (rather than its use for the purposes for which it was intended). In other words, allowing developers of original biological products to benefit, in the broad sense, from both patent and statutory exclusivity regimes might lead to their using the exclusivities under BPCIA for their intended purpose but *misusing* the protection afforded to their products under patent law in a manner that does not comport with the purpose for which patents were created. The measures proposed herein seek to eliminate the risk of such patent abuse by making patent enforcement unavailable in a narrowly defined set of circumstances without derogating from the incentives for R&D of biological products.

²¹³ See *supra* Part IV.B.

²¹⁴ Notably, the 5-11 months term of primary patents beyond the expiration of the market exclusivity period under BPCIA is an *average* number. Thus, while some products would probably be covered by primary patents whose term is more than 5-11 months beyond the market exclusivity period under BPCIA, other products may only be covered by primary patents (if any) whose term is shorter than the market exclusivity period under BPCIA. See *infra* note 219.

²¹⁵ See discussion *supra* Part IV.C.1.

*statutory exclusivities afforded under BPCIA.*²¹⁶ In other words, developers of original biological products would surrender about 5-11 months on average of exclusivity under patent law in return for 12-12.5 years of litigation-free and other legal risks'-free market exclusivity (and 4-4.5 years of data exclusivity).

Further, making it impossible for developers of original biological products to enforce their primary patents against generic applicants filing for generic versions of biological products under BPCIA (including after the expiration of the market exclusivity period) would prevent “double dipping” by developers of original biological products.²¹⁷ Arguably, the length of the market exclusivity period granted under BPCIA²¹⁸ should be sufficient to incentivize R&D in the area of biological pharmaceuticals. There is no justification for “windfalls” in the form of additional monopoly periods conferred by primary patents extending beyond the end of the market exclusivity period in some of the biological products that would further curb public access to these products.²¹⁹

²¹⁶ See discussion *supra* notes 92 and 144 and their accompanying texts.

²¹⁷ To clarify, “double dipping” in this context would be the benefit from both patent and statutory exclusivities regimes in the context of approval of generic biologics under BPCIA.

²¹⁸ The length of the market exclusivity period of 12-12.5 years under BPCIA is in line with the proposals raised by original biologics industry advocates as necessary for the industry to maintain proper incentives for R&D. See *supra* notes 72-73 and accompanying text.

²¹⁹ *E.g.* of the seventy-nine products listed in Table 1, the term of the primary patents covering 53 of them would extend beyond the end of the twelve-year market exclusivity while the term of the primary patents covering 26 of them would not (the ratio shifts to 49 to 30 for a market exclusivity period of 12.5 years).

Importantly, primary patents covering biological products (which would, under the proposal herein, be unenforceable against generic manufacturers seeking approval of their products under BPCIA) would still be enforceable against independent developers of the same biological product and third parties who do not seek to utilize the BPCIA framework and who would therefore not be subject to BPCIA’s statutory exclusivities provisions.

The proposed amendment is unlikely to discourage continued R&D of approved biological products (which is intended to lead to improvements of approved biological products and, possibly, to the development of new ones).²²⁰ This is because the proposed amendment would only apply to patents that cover biological products as originally approved by the FDA.²²¹ To avoid unnecessary legal disputes there may also be merit in explicitly limiting the proposed amendment so that it would only apply to primary patents and would not prevent enforcement of secondary patents covering inventions stemming from continued R&D.²²² Such explicit limitation, while potentially opening the door to abundant litigation involving secondary patents (with all of its risks of evergreening and patent abuse), would assist in providing the necessary incentive for continued R&D of already-approved biologics, which is currently missing from

²²⁰ It is common in the context of pharmaceuticals that primary patents applied for early in a product's development process are followed by additional patents claiming (1) particular ways of formulating the product, (2) additional methods of manufacturing the API or any of the intermediate compounds involved in making it and (3) additional methods of using the product or API for treating additional medical conditions [hereinafter "secondary patents"]. For example, the biologic Enbrel, which was originally approved for the treatment of rheumatoid arthritis, later proved effective in the treatment of other autoimmune diseases such as psoriasis and Crohn's disease and Avastin, which was originally approved for treatment of colorectal cancer, was later approved for treating non-small cell lung cancer and breast cancer. See Grabowski & DiMasi 2009, *supra* note 5, at 4-5 (arguing that new indications are an important source of innovative advances in biologics); Grabowski 2009, *supra* note 5, at 4 (reviewing three drugs approved for one condition which were later approved for other conditions).

²²¹ In the "softer" version, BLA holders should be estopped only from enforcing patents covering the original formulation of the approved biologic, the originally approved indications, the original structure of the biological API, etc.

The author is aware that in leaving an opening for additional monopoly periods subsequent to the expiration of the 12-12.5-year statutory exclusivity period in biological products there remains a risk of abuse by evergreening which would likely need to be addressed in litigation.

²²² Since there is clear societal interest in encouraging such continued R&D, there is merit in offering additional incentives for such research in the form of either patents or statutory exclusivities. As explained earlier, statutory exclusivities under BPCIA are unavailable for most types of modifications of a previously-approved biological product. See *supra* notes 202-204 and accompanying text. Yet, patents may still be available—limited and insufficient as they might be—as a means of incentivizing invention, investment in R&D and disclosure of technology in the context of pharmaceuticals. See *supra* Parts IV.C.1(a), IV.C.1(b) and IV.C.1(d). By limiting the proposed amendments to primary patents, it would be possible to preserve patents as means of encouraging further R&D of already-approved biological products.

BPCIA. An alternative solution to the problem of lack of incentive for continued R&D of already-approved biological products would be to amend 42 U.S.C. § 262(k)(7)(C)(ii)(II) so as to allow for an additional short period of market exclusivity for the approval of additional medical indications for already-approved biological products similar to that afforded under the 3-year additional statutory exclusivity period granted under the Hatch-Waxman Act.²²³

The proposed amendment could also raise concerns that the limitations it imposes on patent recourse might contradict undertakings by the United States under patent treaties not to deny patent protection to classes of technologies as such.²²⁴ However, arguably, the proposed amendment would not deny protection but rather create a *quid pro quo* arrangement wherein in order to benefit from statutory exclusivities under BPCIA, developers of biological products would only be limited in enforcement of their (undeniable) patent rights under a narrow set of circumstances.²²⁵

Finally, the proposed amendment would not seem to be at odds with Article I, Section 8, Clause 8 of the Constitution²²⁶ as the Constitutional language does not grant a positive right to

²²³ See *supra* notes 29 and 204 and accompanying text.

²²⁴ For example, the North American Free Trade Agreement (NAFTA) and the Trade-Related Aspects of Intellectual Property Rights of the World Trade Organization (TRIPS) both stipulate that “each Party shall make patents available for any inventions, whether products or processes, in all fields of technology.” See North American Free Trade Agreement (NAFTA), Dec. 17, 1992, art. 1709(1), 32 I.L.M. 605; The General Agreement on Tariffs and Trade Uruguay Round Agreement on Trade-Related Aspects of Intellectual Property Rights Including Trade in Counterfeit Goods (“TRIPS”), Apr. 15, 1994, art. 27(1), 1994 WL 1711191 (Trty.). See also 2000 CRS Report at 26-27 (“[t]he potential for limiting the patentability of living inventions is moderated by several factors. One source of restraints consists of international agreements to which the United States is a signatory.”).

²²⁵ Notably, this challenge, too, could be overcome by adopting the “softer” version of the proposed amendment under which it would be developers of biological products who would have the option to pursue their rights under patent law *or* benefit from the statutory exclusivities scheme under BPCIA.

²²⁶ See U.S. Const. Art. I § 8 Cl. 8 ([The Congress shall have Power t]o promote the Progress of Science and useful Arts, by securing for limited Times to . . . Inventors the exclusive Right to their . . . Discoveries”). See *id.*

obtain patents as such. Rather, Article I, Section 8, Clause 8 authorizes Congress to devise means of promoting the progress of science and useful arts as it sees fit, which is exactly what BPCIA does and would continue to do with the proposed amendment.²²⁷ Furthermore, if the legal situation remains at its present state, and developers of biological products continue to be able to utilize both patents and statutory exclusivities concurrently to protect their proprietary interests in their products, one could argue that the cumulative protection afforded in biological products is too strong and operates *to obstruct the progress of science and useful arts* in abrogation of Section 8, Clause 8 of the Constitution.²²⁸

5. Why Patents Still Have a Role to Play in Incentivizing R&D in Biologics

The above conclusions and proposed amendment raise the following question: if statutory exclusivities are so clearly preferable to patents in the context of biological products and if patents are not only deficient but possibly even harmful to the interests of developers of biological products and public interest alike, wouldn't it simply be better to forego patent protection in biological products altogether?

The answer to this question is in the negative. Despite their numerous shortcomings and the clear advantages statutory exclusivities have over them, patents still have important functions

²²⁷ Once again, the “softer” version of the proposed amendment could resolve any constitutional difficulty that may arise in this regard under more conservative constitutional construction. Namely, even if one is to construe Article I, Section 8, Clause 8 of the Constitution narrowly as only granting Congress the ability to “secure[] . . . to . . . Inventors . . . exclusive Rights” (rather than deny such rights), under the proposed amendments inventors would choose to benefit from statutory exclusivities by electing to refrain from enforcing their patents. In other words, it will not be Congress that would deny the inventors’ ability to “secur[e] . . . exclusive [r]ights,” but rather the inventors themselves who will be making the choice to limit their own already “secure[d] . . . exclusive [patent r]ights” in exchange for the ability to benefit from the statutory exclusivities afforded under BPCIA.

²²⁸ Such arguments could rely on the various ways in which patents could be abused and misused in an anti-competitive manner. See *supra* Part IV.C.2(b). Notably, a constitutional analysis of Congress’s power to create the statutory exclusivity scheme under BPCIA appears to merit further analysis, which exceeds the scope of this Article.

to fulfill in incentivizing the development of biological products during the period *prior to the approval of biological products by the FDA*. Patents serve an important fundraising tool, which enables R&D entities to raise the funds necessary to support their research projects.²²⁹ In this respect patents have a vital function in the development of pharmaceutical products and, even more so, of biological products—given their high R&D costs—as they make it possible for developers of such products to raise the funds necessary to traverse the various, numerous expensive steps of clinical development prior to being eligible to benefit from the statutory exclusivities under BPCIA (subsequent to approval of the biological product by the FDA).

A possible explanation of the “sway” patents may have in convincing investors to commit funds to certain R&D projects is their ability to prevent situations of a “race to register.”²³⁰ In this respect, patents serve not only as a signaling device between companies but also as means of blocking one’s competitors from entering into such a “race to register” in the first place. This explanation appears to be especially valid in the context of the biologics industry which consists of a significant portion of small to medium R&D firms. In “race to register” situations, patents would improve the survivability of such small to medium R&D firms competing against major pharmaceutical corporations during the development stages of biological products prior to their approval by the FDA.²³¹ Thus, patents would make it possible

²²⁹ Although patents may not provide any additional monopoly period to that afforded by the statutory exclusivities under BPCIA or directly attest to the prospects of success of an R&D project that may lead to a biological product, patents carry substantial weight with investors.

²³⁰ A “race to register” occurs when two companies undertake a similar research project and are competing to have their respective products approved by the FDA first.

²³¹ Since large corporations usually have more resources, it is expected that with everything else being equal, they will almost always “win” in “race-to-register” situations.

for small to medium R&D outfits to stay in the market to see another day (and, perhaps, another research project).²³²

Accordingly, during the period prior to approval of biological products by the FDA and the onset of statutory exclusivities under BPCIA, patents would actually serve as “insurance policies” that would make the achievement of statutory exclusivities possible further down the road. In addition, as discussed earlier, follow-on patents would also have an important role to play subsequent to the expiration of statutory exclusivity periods under BPCIA.²³³ To summarize: there is merit in affording biological products *sequential (rather than concurrent) protection* from (1) any *primary* patents pertaining to the underlying technology in such products prior to the onset of statutory exclusivities under BPCIA, (2) statutory exclusivities in the FDA approved products themselves and (3) any *secondary* patents pertaining to substantial²³⁴ further developments of the originally approved biological product.

V. Statutory Exclusivities in Biological Products—A Peculiar Case or the Future of Incentivizing Innovation

In view of the foregoing conclusions one cannot help but wonder: is the regulation of generic biologics a harbinger of a new type of intellectual property regime wherein patents and statutory-exclusivity work in tandem to incentivize R&D? Can we expect to see similar regimes put in place with respect to other areas of technology? And are there areas of technology in

²³² Alternatively, early patent applications and patents issued from them would make it possible for small-medium R&D firms to get, at the very least, through the initial proof-of-concept or pre-clinical testing stages that would enable them to sell their research project to major pharmaceutical corporations.

²³³ See *supra* notes 220-223 and accompanying text.

²³⁴ Notably, the inclusion of the “substantiality” language is meant to clarify that sequential protection of insubstantial developments of the biological product—which are essentially evergreening—are not within the scope of legitimate sequential patent protection described herein.

which it would be desirable to replace the traditional patent regime with a new regime of statutory exclusivities altogether? As the pattern of technical advance varies significantly from field to field and from one industry to another,²³⁵ statutory exclusivity frameworks would not necessarily be similarly suitable for all fields and industries. However, it is quite possible that because of their lower transaction costs and the legal certainty they provide statutory exclusivities could complement patents in some areas of technology and possibly even obviate patents altogether in others. It would thus be beneficial to make some observations regarding the characteristics of areas of technology that may be “candidates” for such a change in technology-protection regime.²³⁶

Yet, before making any such observations, it is worth highlighting two “pre-requisites” for the administration of statutory exclusivities’ regimes. First, to be a “candidate” for implementation of a statutory exclusivity framework—just like in the area of pharmaceuticals—a technological area must be subject to regulation by a dedicated and qualified impartial body, e.g. an executive agency, capable of administering the regulatory framework instituting the exclusivities regime. Such a body ought to routinely regulate the pertinent technological area or have direct bearing to that particular area and must have a substantial amount of expertise in evaluating technologies in that area. Given its particular expertise, arguably, such a body would be better suited than the USPTO to evaluate relevant technologies in its area of expertise and

²³⁵ See Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 Colum. L. Rev. 839, 880 (1990).

²³⁶ Notably, such an approach is in concert with the Federal Circuit’s general approach of adapting the legal framework to particular areas of technology. See Aljalian, *supra* note 168, at 18-19 (“patent scope has come to be largely dependent on the technology at issue. The Federal Circuit actively tailors patent law and policy to the technology under consideration. This new approach is viewed as having ‘a significant impact’ on advances in technology and various industries.”).

would therefore be in a better position to make merit assessments with respect to such technologies from a public benefit perspective.

A second prerequisite for the implementation of statutory exclusivities regimes is that the practical application of technology in the regulated area would require some kind of regulatory approval or the removal of a regulatory bar. This requirement is essential for the administration of statutory exclusivities regimes because it is the withholding of the approval to use the technology or the imposition of the regulatory bar that would effectuate the exclusivities. Notably, once a technological area is recognized as a potential candidate for the implementation of a statutory exclusivity framework, it would be possible to fulfill the aforementioned prerequisites—the regulation of the technological area by a dedicated and qualified impartial body and the existence of a requirement for regulatory approval or removal of a regulatory bar in order to put technology in that area into practical application—via appropriate legislation.

Statutory exclusivities regimes would be, primarily, suitable in areas of technology in which (1) additional incentives to invent/invest are necessary because the existing incentives provided under patent law are insufficient, and/or (2) the circumstances of the particular market pertaining to the regulated technological area lend themselves to inefficiencies such as abuse of market share. Statutory exclusivities regimes ought *not to* be considered in areas that do not call for additional incentives, *e.g.*, areas in which development of technology is relatively cheap, does not require substantial amounts of know-how and expertise or the risks of not recouping one's investments are low.²³⁷ Ideally, statutory exclusivities regimes should be implemented in

²³⁷ Awarding statutory exclusivities in areas that do not require further incentives to invent, invest in R&D or disclose technology might work to achieve the opposite results.

technological areas that have high entry barriers—financial, technological or both—and where the prospects of return on investment are unpredictable or involve substantial risks.

As for the question of when, if ever, should statutory exclusivities replace patents altogether, it is difficult to establish a bright line rule regarding the circumstances which would necessitate and justify such replacement. However, as stated above, it is possible to propose some parameters that would, potentially, assist in identifying technological areas which may be suitable for excepting technology from protection under patent law in favor of protection under a statutory exclusivities regime. Presumably, these areas would be such that exhibit extreme cases of the aforementioned characteristics, namely where patent protection provides very little to no incentives (or even negative incentives²³⁸) to invent/invest or to disclose new technology and/or where the market in the technology which utilizes the pertinent technology is plagued by constant inefficiencies. Statutory exclusivities may be especially fitting as replacement for patents in technological areas that are particularly susceptible or prone to patent abuse.

Notably, the implementation of statutory exclusivities regimes itself is also not devoid of risks of inefficiencies and abuse. With statutory exclusivities regimes being based on reliance on expert regulators, risks of regulatory/agency capture become more prominent.²³⁹ In the context of approvals of pharmaceutical products by the FDA, for example, this risk is evident in the fact that FDA personnel is in regular contact with representatives of certain corporations who are

²³⁸ Hypothetically, there could be areas of technology where the traditional patent regime is so deficient that it actually creates negative incentives to invent/invest and/or disclose, in which case patent protection should be forgone and a statutory exclusivities regime ought to be made the sole method of protecting technology.

²³⁹ Regulatory/agency capture occurs when a regulatory body or agency created to regulate certain industries or sectors in the public interest, instead, advances the commercial or special interests of the industries or sectors of which it is charged with regulating.

prominent and repeated actors in the regulated area and who are also, frequently, former members of the FDA themselves. Being aware of such risks of regulatory/agency capture is therefore essential for making sure that there are sufficient checks within agencies that are to administer statutory exclusivities regimes and which may be provided for by appropriate institutional design.²⁴⁰

Example of areas that meet the above criteria and may be suitable for the application of statutory exclusivities in addition to or in lieu of patents are the regulation of foods, cosmetics, veterinary pharmaceuticals and vaccines,²⁴¹ medical devices²⁴² and diagnostics and plant breeds.²⁴³ It is quite possible that technological advancements in other areas and regulation thereof would render more and more areas of technology candidates for supplementation (or, possibly even replacement) of the traditional patent regime with statutory exclusivities.

VI. Conclusion

The most important function of patents and statutory exclusivities alike is to ensure that those partaking in technological R&D would not only survive to continue their activity but would also prosper and seek to continue their R&D activities in the future. However, in some technological areas, patents might not serve this purpose as well as statutory exclusivities would.

²⁴⁰ See generally Rachel Barkow, *Insulating Agencies: Avoiding Capture Through Institutional Design*, 89 Tex. L. Rev. 15 (2010).

²⁴¹ See generally http://www.aphis.usda.gov/animal_health/vet_biologics/.

²⁴² See generally <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/510kClearances/default.htm>.

²⁴³ Notably, all of these areas are regulated by the Department of Agriculture (DA) and the FDA in the Department of Health and Human Services (DHHS). Unfortunately, the scope of this article does not allow for examination of the potential supplementation (or replacement) of patents with of statutory exclusivities.

This article does not purport to propose a “patentless world” or portray patents as dinosaurs—ancient relics of a once glorious past. As explained above, statutory exclusivities would and should only serve as an addition to patents in a narrow class of well defined circumstances; the emergence of statutory exclusivities should not be perceived as hailing the demise of the patent system. Yet, at least in some technological areas, patents may be a less than preferable way of promoting innovation and should be substituted by statutory exclusivities, where possible.²⁴⁴ Thus, this article advocates the substitution of patent enforcement rights with statutory exclusivities of appropriate lengths in those areas where there is a regulatory body capable of evaluating and granting licenses to partake in activities involving particular types of patentable technologies and in which the public has an interest in encouraging further technological development.²⁴⁵ Biologics represent such a case.

As discussed in this article, in the context of generic biologics the statutory exclusivities instituted by BPCIA make primary patents redundant and, by comparison, an inferior way of ensuring the proprietary interests of developers of biological products in their technology. The statutory exclusivities afforded under BPCIA have been tailored to the needs of developers of

²⁴⁴ See 2008 CRS Report, *supra* note 1, at 18 (recognizing that patents may not be “the most successful mechanism for capturing the benefits of investment” in every industry and arguing that “[t]he utility of patents to companies varies among industrial sectors”).

²⁴⁵ This proposition coincides with Machlup’s belief that

[w]hile the student of the economics of the patent system must, provisionally, disqualify himself on the question of the effects of the system *as a whole* on a large industrial economy, he need not disqualify himself as a judge of proposed *changes* in the existing system. While economic analysis does not yet provide a basis for choosing between “all or nothing,” it does provide a sufficiently firm basis for decisions about “a little more or a little less” of various ingredients of the patent system.

See Machlup, *supra* note 11, at 80.

biological products in the context of generic competition and should thus be held as sufficient for accommodating those needs. Allowing developers of biological products to benefit from the protection of primary patents alongside and concurrent with such statutory exclusivities would cause waste and could lead to abuse of the patent system. Further, it is important to remember that patents, despite their long legal history and well known status as instruments of incentivizing innovation, are only a means to an end. Assuming this “end” is as well or even better served by other means (*e.g.* statutory exclusivities), patents may lose their allure and become redundant, and possibly even harmful. A substitution of primary patent enforcement rights where statutory exclusivities in FDA-approved biological products are in force is the best means to incentivize continued investment in R&D while guaranteeing sufficient public access to generic versions of biological products.

Appendix A

Table 1²⁴⁶

I	II	III	IV	V	VI	VII	VIII
Biological product (and API)	U.S. Patent No.	Patent application filing date ²⁴⁷	FDA approval date	Patent expiration date ²⁴⁸	twelve-year market exclusivity expiration date ²⁴⁹	Time from patent application to FDA approval ²⁵⁰	Time from expiration of patent term to end of twelve-year market exclusivity ²⁵¹
Activase® (alteplase)	4766075	5/5/1982	6/18/1996	8/23/2005	6/18/2008	5158	1030
Aldurazyme® (laronidase)	6426208	11/12/1999	4/30/2003	11/12/2019	4/30/2015	1265	-1657
Amevive® (Alefacept)	5547853	3/12/1991	1/30/2003	1/30/2017	1/30/2015	4342	-731
Angiomax® (bivalirudin)	5196404	8/18/1989	12/15/2000	3/23/2010	12/15/2012	4137	998
Apidra® (insulin glulisine)	6221633	6/18/1998	4/16/2004	6/18/2018	4/16/2016	2129	-793
Aranesp™ (darbepoetin alfa)	5856298	10/13/1989	9/17/2001	1/5/2016	9/17/2013	4357	-840
Arcalyst® (Rilonacept)	5470952	10/20/1993	2/27/2008	11/28/2012	2/27/2020	5243	2647
Avastin™ (bevacizumab)	6884879	4/7/1997	2/26/2004	4/7/2017	2/26/2016	2516	-406
Avonex® (interferon beta-1a; recombinant)	4530901	2/4/1980	5/17/1996	7/23/2002	5/17/2008	5947	2125
BeneFix™ (coagulation factor IX)	5171569	3/13/1986	2/11/1997	2/11/2011	2/11/2009	3988	-730
Betaseron® (Interferon beta-1b)	4588585	10/19/1982	7/23/1993	7/7/2007	7/23/2005	3930	-714
Bexxar® Therapeutic Regimen (Tositumomab and Iodine I-131 Tositumomab)	5595721	9/16/1993	6/27/2003	1/21/2014	6/27/2015	3571	522
Byetta® (exenatide)	5424286	5/24/1993	4/28/2005	12/1/2016	4/28/2017	4357	148
Cerezyme® (imiglucerase)	5236838	12/23/1988	5/23/1994	8/17/2010	5/23/2006	1977	-1547
Cimzia® (Certolizumab pegol) 200 mg/ml	7094872	2/19/2004	5/13/2009	7/6/2024	5/13/2021	1910	-1150
Elaprase® (Idursulfase)	5932211	11/12/1991	7/27/2006	9/3/2019	7/27/2018	5371	-403
Elitek® (rasburicase)	5382518	7/13/1990	7/12/2002	7/12/2016	7/12/2014	4382	-731

²⁴⁶ All times are in days; all time difference calculations were conducted using date calculation tools available at <http://www.timeanddate.com/>.

²⁴⁷ Filing date is the patent application effective U.S. filing date for term calculation purposes.

²⁴⁸ Patent expiration date includes any term extensions and adjustments.

²⁴⁹ Calculated by adding 12 years to the date of FDA approval (column IV).

²⁵⁰ Calculated as the difference in days between the FDA approval date (column IV) and the patent application filing date (column III).

²⁵¹ Calculated as the difference in days between the twelve-year market exclusivity expiration date (column VI) and the patent expiration date (column V).

I	II	III	IV	V	VI	VII	VIII
Biological product (and API)	U.S. Patent No.	Patent application filing date ²⁴⁷	FDA approval date	Patent expiration date ²⁴⁸	twelve-year market exclusivity expiration date ²⁴⁹	Time from patent application to FDA approval ²⁵⁰	Time from expiration of patent term to end of twelve-year market exclusivity ²⁵¹
Enbrel® (etanercept)	RE36755	9/5/1989	11/2/1998	10/23/2012	11/2/2010	3345	-721
Epogen® (epoietin alfa)	4703008	12/13/1983	6/1/1989	10/27/2004	6/1/2001	1997	-1244
Erbitux™ (cetuximab)	7060808	6/7/1995	2/12/2004	6/7/2015	2/12/2016	3172	250
Fabrazyme® (agalsidase beta)	5356804	10/24/1990	4/24/2003	9/27/2015	4/24/2015	4565	-156
Forteo® (teriparatide)	4698328	4/4/1985	11/26/2002	4/4/2005	11/26/2014	6445	3523
Fuzeon™ (Enfuvirtide)	6133418	6/7/1993	3/13/2003	11/17/2014	3/13/2015	3566	116
Geref® (sermoreline acetate)	4703035	10/4/1982	12/28/1990	12/28/2004	12/28/2002	3007	-731
Gonal-F® (follitropin alfa)	5156957	11/2/1983	9/29/1997	9/29/2011	9/29/2009	5080	-730
Herceptin® (trastuzumab)	5677171	1/12/1988	9/25/1998	10/14/2014	9/25/2010	3909	-1480
Humira™ (adalimumab)	6090382	2/9/1996	12/31/2002	12/31/2016	12/31/2014	2517	-731
Ilaris® (Canakinumab)	7446175	8/20/2001	6/17/2009	12/22/2022	6/17/2021	2858	-553
Increlex™ (mecasermin)	5681814	6/7/1990	8/30/2005	9/18/2017	8/30/2017	5563	-19
Infergen® (interferon alfacon-1)	4695623	5/6/1982	10/6/1997	9/22/2009	10/6/2009	5632	14
Intron A® (alpha-interferon)	4496537	12/23/1981	6/4/1986	1/29/2002	6/4/1998	1624	-1335
Iplex™ (mecasermin rinfabate [rDNA origin])	5681818	3/31/1988	12/12/2005	5/11/2019	12/12/2017	6465	-515
Kepivance® (palifermin)	5677278	6/29/1993	12/15/2004	10/14/2014	12/15/2016	4187	793
Kineret™ (anakinra)	5075222	5/27/1988	11/14/2001	12/24/2013	11/14/2013	4919	-40
Lantus® (insulin glargine)	5101013	8/9/1988	4/20/2000	12/3/2011	4/20/2012	4272	139
Leukine® (Sargramostim - granulocyte macrophage colony-stimulating factor)	5391485	8/6/1985	3/5/1991	2/21/2012	3/5/2003	2037	-3275
Lucentis® (Ranibizumab)	6884879	4/7/1997	6/30/2006	4/7/2017	6/30/2018	3371	449
Luveris® (lutropin alfa for injection)	5639639	11/2/1983	10/8/2004	6/20/2011	10/8/2016	7646	1937
Macugen® (pegaptanib)	6051698	6 June 1997	12/17/2004	5/19/2015	12/17/2016	2751	578
Mircera® (Methoxypolyethylene glycol epoetin beta)	6583272	6/27/2000	11/11/2007	8/26/2020	11/11/2019	2697	-289
Myobloc® (Botulinum Toxin Type B)	6290961	12/28/1993	8/12/2000	12/28/2013	8/12/2012	2419	-503
Myozyme® (Alglucosidase alfa)	7351410	12/6/1999	4/28/2006	10/29/2020	4/28/2018	2335	-915
Naglazyme® (Galsulfase)	6972124	5/1/2000	5/31/2005	7/17/2020	5/31/2017	1856	-1143
Natrecor® (nesiritide)	5114923	5/31/1988	8/10/2001	5/19/2014	8/10/2013	4819	-282
Neulasta™ (pegfilgrastim)	5582823	8/23/1985	1/31/2002	12/10/2013	1/31/2014	6005	52
Neumega® (oprelvekin)	5215895	11/22/1989	11/25/1997	11/25/2011	11/25/2009	2925	-730
Neupogen® (filgrastim)	4810643	8/23/1985	2/20/1991	3/7/2006	2/20/2003	2007	-1111
Nplate® (Romiplostim)	6835809	10/22/1999	8/22/2008	10/22/2019	8/22/2020	3227	305
Orencia™ (abatacept)	5851795	6/27/1991	12/23/2005	11/25/2017	12/23/2017	5293	28
Orthoclone OKT3® (muromonab-CD3)	4361549	4/26/1979	9/14/1992	11/30/1999	9/14/2004	4890	1750

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Ovidrel® (human chorionic gonadotropin)	4840896	11/2/1983	9/20/2000	4/29/2009	9/20/2012	6167	1240
PEG-Intron™ (pegylated interferon alfa-2b)	5951974	11/10/1993	1/19/2001	1/19/2015	1/19/2013	2627	-730
Proleukin, IL-2® (aldesleukin)	RE33653	10/19/1982	5/5/1992	5/5/2006	5/5/2004	3486	-730
ProstaScint® (Capromab Pendetide)	5162504	6/3/1988	10/28/1996	10/28/2010	10/28/2008	3069	-730
Raptiva™ (efalizumab)	6037454	11/20/1997	10/27/2003	11/20/2017	10/27/2015	2167	-755
ReFacto® (antihemophilic factor)	4868112	4/12/1985	3/1/2000	2/28/2010	3/1/2012	5437	732
Regranex® (Becaplermin)	4845075	2/25/1985	12/16/1997	10/29/2010	12/16/2009	4677	-317
Remicade® (infliximab)	5656272	3/18/1991	8/24/1998	8/12/2014	8/24/2010	2716	-1449
Remodulin™ (treprostinil sodium)	5153222	6/16/1989	5/21/2002	10/6/2014	5/21/2014	4722	-138
Retavase™ (reteplase)	5223256	2/6/1990	10/30/1996	10/30/2010	10/30/2008	2458	-730
Rituxan™ (rituximab)	5763137	7/29/1996	11/26/1997	7/29/2016	11/26/2009	485	-2437
Roferon (Interferon alfa-2a)	4503035	11/24/1978	4/6/1986	3/5/2002	4/6/1998	2690	-1429
Simlect® (Basiliximab)	6521230	3/14/1991	12/5/1998	2/18/2020	12/5/2010	2823	-3362
Soliris® (Eculizumab)	6074642	5/2/1994	3/16/2007	5/2/2014	3/16/2019	4701	1784
Somavert® (pegvisomant)	5849535	9/21/1995	3/25/2003	3/25/2017	3/25/2015	2742	-731
Stelara™ (Ustekinumab)	6902734	8/1/2001	9/25/2009	7/26/2022	9/25/2021	2977	-304
Synagis™ (palivizumab)	5824307	12/23/1991	6/19/1998	10/20/2015	6/19/2010	2370	-1949
Tarceva® (Erlotinib)	5747498	6/6/1995	11/18/2004	11/8/2018	11/18/2016	3453	-720
Thyrogen® (thyrotropin alfa)	5240832	6/20/1989	11/30/1998	8/31/2010	11/30/2010	3450	91
TNKase™ (tenecteplase)	5385732	5/20/1988	6/2/2000	6/2/2014	6/2/2012	4396	-730
Tysabri® (natalizumab)	5840299	1/25/1995	11/23/2004	4/27/2017	11/23/2016	3590	-155
Vectibix® (Panitumumab)	6235883	5/5/1997	9/27/2006	5/5/2017	9/27/2018	3432	510
Velcade™ (bortezomib for injection)	5780454	10/28/1994	5/13/2003	5/3/2017	5/13/2015	3119	-721
Verluma (Nofetumomab)	4897255	1/14/1985	10/13/1998	8/20/2010	10/13/2010	5020	54
Visudyne™ (verteporfin for injection)	5095030	1/20/1987	4/12/2000	9/9/2011	4/12/2012	4831	216
Xigris™ (drotrecogin alfa)	RE37806	4/9/1986	11/21/2001	11/21/2015	11/21/2013	5705	-730
Xolair® (omalizumab)	6267958	3/14/1996	6/20/2003	6/20/2017	6/20/2015	2654	-731
Zenapax (Daclizumab)	5530101	12/28/1988	10/12/1997	6/25/2013	10/12/2009	3210	-1352
Zevalin™ (ibritumomab tiuxetan)	5776456	11/13/1992	2/19/2002	2/19/2016	2/19/2014	3385	-725
Average						3728.35	-326.95